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PUBLIC HEALTH

1678. **The Medical Results of the Occupation of France.** (Les conséquences sanitaires de l'occupation en France) G. HENRI. *Lékařské Listy* [*Lék. Listy*] **1**, 488–490, Oct. 15, 1946.

Famine oedema appeared in occupied France late in 1940; during that year most of the population suffered from dietary deficiencies. The ordinary person had to subsist on a diet of 1,000 calories; the manual labourer had one of 1,500. Homes for the aged, asylums, camps, prisons, and colleges were reduced to a starvation diet. In one asylum there were at least 12 deaths a day from starvation. The mean cuts in diet were:—for children 23%, adolescents 42%, adults 60%, and old people 55%. The theoretical rations of 125 g. of meat a week and 300 g. of fat per month were seldom attained. Personal hygiene was at a low level because of the shortage of soap and linen. Loss of weight was general, 5 to 10 kg. being a usual and 20 to 30 kg. an extreme loss. Children of all ages showed grave departures from the normal in height and weight.

Famine oedema appeared among inmates of various institutions after 4 to 6 months of reduced rations. It was seen particularly among men over the age of 50, and depended not only on calorie shortage but also on the shortage of fats and proteins in a diet consisting largely of cabbages, carrots, and turnips. Polyuria, low body temperature, bradycardia, asthenia, and wasting were followed by general anasarca with effusions, an increase in the total quantity of blood and body fluids being demonstrated. Amenorrhoea associated with uterine involution and alimentary disturbances including peptic ulcers were recorded, as well as spontaneous fractures and deformities due to late rickets. Intractable hypoglycaemic coma was seen where the degree of malnutrition was extreme. The author states, however, that conditions due to actual vitamin deficiencies were limited to those resulting from deficiency of nicotinic acid. Skin manifestations were rare, but an itchy erythema with gingivitis, pharyngitis, and hyperchlorhydria was observed.

These dietary deficiencies were followed by a flare-up of infectious diseases among which typhus appeared even in Paris but was unimportant; prophylactic measures were adopted early, Giroud using emulsions of rickettsiae recovered from rabbit's lung, a technique much simpler than the employment of the chick embryo. As regards tuberculosis, not only was the disease aggravated in those already suffering from it, but there were many new cases. Repatriated prisoners of war and deported and starving populations exhibited similar manifestations, including a particularly virulent bronchopneumonia, peritonitis, pleurisy, and pericarditis of a grave character. In 1941, mortality from tuberculosis was 30% above pre-war rates. Parasitic skin disease, especially scabies, greatly increased, the number of patients treated at the Saint Louis Hospital rising from 10,000 annually in pre-war years to 100,000 in 1942.

W. N. Pickles

1679. **British Commonwealth Scientific Official Conference, London, 1946. Report of Proceedings.** H.M. Stationery Office, London, 1946. 73 pp.

In July, 1946, a conference was held to discuss scientific questions affecting the British Empire. A number of recommendations and resolutions of medical interest were passed dealing with: (1) the physiological and psychological factors affecting human life under tropical conditions and in industry; (2) the aetiology and control of infections and transmissible diseases; and (3) nutrition with special reference to the particular problems of the Empire, including the nutritional status of the indigenous peoples of the Colonies.

It was recommended that laboratories for physiological and psychological research should be established at suitable centres in Africa and the Far East. Research on output in industry in the tropics is required, as data are practically non-existent. An authoritative guide on standards for building—domestic and industrial—is desirable. A co-ordinating Empire Committee on Human Climatology should be set up.

The Conference felt that there were grave dangers of spread of infectious diseases from one part of the Empire to another, and within certain Empire countries. Particular attention was drawn to malaria, yellow fever, schistosomiasis, trypanosomiasis, plague, cholera, and diseases spread by sand flies. More knowledge of the oecology of infectious diseases, their arthropod vectors, and the reasons for the persistence of infection in localized endemic areas is needed. The attention of universities and other authorities should be drawn to the need in many parts of the Empire for oecologists and entomologists, both medical and non-medical. It was specially recommended that an international organization should be established under U.N.O. which would be concerned with the prevention of the spread of diseases from endemic to non-endemic areas. Such an organization would: (*a*) Control vaccination and inoculation in connexion with diseases to which these or other such precautions might be held to be applicable. (*b*) Ensure

the freedom of aeroplanes, aerodromes, ships, and other facilities for travel between different countries, from insects and other media of infection. (*c*) Secure uniformity in regulations regarding certificates required by travellers between different countries. (*d*) Devise such methods of administration as would avoid vexatious and unnecessary impediments to the movement of travellers or goods.

The Conference noted that existing regulations at airports and other transit centres are unsatisfactory owing to a shortage of trained sanitary inspectors and medical personnel. For the prevention of spread of certain diseases from endemic to non-endemic areas within particular countries the Conference urged that local and permanent organizations were required for containing and controlling the diseases in the endemic areas. Particular reference was made to cholera and plague.

The Conference also urged the necessity for developing at all levels of Colonial Government a proper awareness of the nutritional requirements of the indigenous peoples. It strongly supported the need for integrating the efforts of producer, consumer, technical and administrative personnel in effecting improvements in nutrition. It also agreed on the evidence for malnutrition in the Empire, both as to quantity and quality, and recommended application of certain remedial measures. These special recommendations were the immediate therapy of vitamin deficiency diseases—vitamin B_1 for beriberi in Malaya and Hong Kong [Freetown might also be added]; iodine in goitrous areas in Nigeria [and Gold Coast]; calcium and vitamin D where rickets occurs in the Gold Coast; iron where anaemia is common, especially in British Guiana.

The need for more food technologists was urged to improve methods of storing, processing, and distributing foodstuffs and improve milling of wheat and maize, parboiling of rice, drying of fish, fruit, and vegetables. Increased production of " protective foods " was essential by the control of livestock diseases, improved animal husbandry and animal breeding, and better fishing operations. Increased food production by the greater use of fertilizers and by the extension of plant breeding was necessary.

[The Conference did not, unfortunately, urge the need for propaganda for a mixed diet. Many indigenous people think it disgusting to partake of eggs or milk. Rice eaters do not like millet; millet eaters turn up their noses at yams and cassava.]

G. M. Findlay

1680. **The Efficacy of Insecticidal Sprays in Aircraft**
P. C. C. Garnham. *East African Medical Journal* [*E. Afr. med. J.*] **23**, 272–277, Sept., 1946. 4 refs.

The disinfestation of aeroplanes at the time of their arrival is unsatisfactory, because the mooring hatch and the pilot's window have to be opened before the machine can tie up. At Kisumu, where the experiments were carried out, all departing and arriving planes were sprayed. To estimate the efficiency of the methods and of the insecticides used cages containing live mosquitoes were placed in various parts of the plane. Of the seven solutions tested " Freon bombs " and paraffin extract of Kenya pyrethrum, 1 lb. (0·45 kg.) to the gallon (4·5 litres), proved the quickest killers, but the pyrethrum solution, to be effective, had to be freshly prepared. The authors found that all parts of a flying boat were " accessible to insecticides, if used in sufficient concentration, with the unimportant exception of the bullion lockers ". It was observed, however, that mosquitoes protected by a layer of thin cloth remained largely unaffected by any except unusually high concentrations. That this observation is of considerable practical importance is shown by the fact that a proportion of *Aëdes aegypti*, resting in the empty sleeve of a raincoat, remained in their shelter even when the garment was subjected to considerable handling, and that when thus protected they were virtually immune to the action of the insecticides used.

R. M. Gordon

1681. **Design and Planning of Sanatoria**
W. E. Snell. *Monthly Bulletin of the Ministry of Health and the Emergency Public Health Laboratory Service* [*Mon. Bull. Min. Hlth*] **5**, 250–258, Dec., 1946. 2 figs.

The concept of sanatorium design has changed with current medical thought and practice; it must now include not only the " open-air " principle but also provide in structure and equipment all the resources of a first-class general hospital. Such an institution might treat all types of chest disease, not only tuberculosis. It should have at least 250 beds, and preferably 500 beds if both sexes and all types of cases of tuberculosis, as well as cases of non-tuberculous chest disease, are admitted. Its site should not be too remote and should have 30 to 40 acres of well-laid-out grounds sloping to the south or south-west. All wards should also face south or south-west; this necessitates a multi-storied building if reasonable compactness is to be secured. Each ward should contain about 30 beds, and should be divided into two rooms of 10 beds, one of 5 beds, and five single rooms; in addition there should be a ward-kitchen, a sterilizing room, a clinical room, and sister's office. A service corridor should be provided on the north with sanitary annexes projecting outwards therefrom.

The administrative block should provide on the ground floor an entrance hall and a waiting room for patients' visitors together with offices. From here, also, covered corridors should radiate to separate blocks behind the main structure to provide kitchen facilities, dining halls for ambulant patients and staff, recreation hall, billiard-room, reading and writing rooms and library, and an occupational therapy department. Ancillary departments, such as boiler-house, workshops, bedding-sterilizer, and laundry would also be situated behind, but close to, the main structure. If the sanatorium is close to a centre of population possibly a self-contained out-patient department might also be provided. The upper floors of the administrative block would provide operating theatres, and *x*-ray department, lecture room and laboratories, and possibly a physiotherapy department.

A 500-bed sanatorium would need two main and two minor operating theatres, and the latter should have a waiting room and dressing facilities. If residences are provided for senior members of the staff they should not overlook, or be overlooked by, the ward blocks. Separate road entrances are desirable. The nurses' home should be fitted with comfortable bed-sitting rooms, and be free from petty restrictions. The training-school and class-rooms should not be in the nurses' home.

Finally, the author shows how his suggestions might be applied to the re-planning of a bombed sanatorium, a plan of which accompanies the article.

R. J. Lumsden

1682. **Organization for Old Age. An Institute of Gerontology?**
T. H. HOWELL. *Lancet* [*Lancet*] **1**, 264–265, Feb. 15, 1947.

The care of the aged sick used to be a problem for the relations only; now it concerns the whole community, and organization against old age is long overdue. The sick used to be looked after by the general practitioner. In recent years the municipal " chronic " hospitals have undertaken the care of many, but investigations show that few of these hospitals compare in efficiency with the average general hospital. There is a gulf between the medical and social aspects of gerontology which is being bridged by the Nuffield Foundation; the latter promotes research and collects social welfare data. A number of societies are interested in the care of the aged, among them the National Old People's Welfare Committee, the Old People's Homes Committee of the Family Welfare Association, and the Darby and Joan Club. No fewer than 34 separate bodies are represented on the first of these.

Provision for the aged infirm who need care and supervision at home is insufficient, and there is no central bureau to correlate the functions of the various societies. An attempt at co-ordination on the social side has been started by the National Old People's Welfare Committee, but this does not cover the medical and nursing care of the aged. There is a case for an Institute of Gerontology in Britain which would conduct research into old age, organize teaching, encourage publication of original work on gerontology, and help the establishment of special hospital units in selected centres. On the social welfare side the institute would serve as a central bureau for domestic helps, convalescent homes, and hospital or hostel accommodation. The author concludes: " The young plant of gerontology must be watered and fertilized. All the present interest in the subject must be harnessed while it is still fresh. As for the National Health Service, it is a challenge to act while voluntary initiative can be effective. Before long, every new proposal will have to be referred to the mandarins of Whitehall. An organization in being before 1948 would have a better chance of survival than one arising after that date. . . . The need for it is urgent. . . . Now is the time to act."

A. Michael Critchley

1683. **A Preliminary Note on Smallpox Imported into England during 1946**
E. C. G. MADDOCK and E. T. CONYBEARE. *Monthly Bulletin of the Ministry of Health and the Emergency Public Health Laboratory Service* [*Mon. Bull. Min. Hlth*] **5**, 242–243, Nov., 1946.

The authors have investigated all cases of smallpox occurring in England during 1946, with special reference to the possibility of the introduction of this disease from troopships. Their conclusions are: " Of a total of 55 cases of smallpox, 15 were infected either in India or en route from India. There were 40 cases infected in England, but in only 7 of them could direct connexion with an imported case be established. The remaining 33 cases can be divided into 10 separate outbreaks. All these outbreaks occurred in districts and at times which suggested that their source was shipborne."

A. Michael Critchley

1684. **Insect Tests of Wire Screening Effectiveness**
S. S. BLOCK. *American Journal of Public Health and the Nation's Health* [*Amer. J. publ. Hlth*] **36**, 1279–1286, Nov., 1946. 4 figs., 5 refs.

The author describes experiments with mosquitoes and other insects to test the effectiveness of wire screening with square and rectangular apertures. All the screening tested was made of wire of 0·011 in. diameter, but the meshes investigated were 18×18, 16×16, and 14×14 for square meshes and 18×16, 18×14, and 18×12 for rectangular meshes. The majority of the tests were carried out with laboratory bred mosquitoes—*Anopheles quadrimaculatus*, *A. quinquefasciatus*, and *Aëdes aegypti* —in cages 12×4×2 in., made of the screening under test; the cases were placed in gauze-covered museum jars. After 48 hours the mosquitoes were gassed and a count made of those inside and outside the cages. None of the meshes permitted the escape of *A. quadrimaculatus* or *A. quinquefasciatus*, but undersized *Aëdes aegypti* escaped through all the meshes and normal-sized *A. aegypti* through most. The percentage of *Aëdes* escaping was found to be directly proportional to the length of the diagonal of the apertures. Screening having a mesh of 18×14 proved to be as effective as screening with a mesh of 16×16. The placing of the rectangular aperture with the long axis vertical was important, since in 18×12 mesh a greater proportion of *Aëdes* escaped when the long axis was horizontal. The effectiveness of different meshes against small light-attracted insects (gnats, tiny moths) was studied, and in these also the proportion of penetrations was directly related to the length of the diagonal of the aperture. Only 18×18 or finer mesh acted as an appreciable barrier to these small insects.

[This is a careful study of the comparative effectiveness of wire screening with the rectangular or the square apertures. The former is more rapidly woven and should therefore be cheaper. No reference is made to British literature on the greater importance of aperture measurements as compared with mesh counts.]

T. H. Davey

1685. **An Outbreak of Staphylococcal Food Poisoning. The Possible Source Traced by Means of Bacteriophage Typing**

E. H. GILLESPIE. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* [*Mon. Bull. Min. Hlth*] **6**, 8–10, Jan., 1947.

This paper describes an outbreak of staphylococcal food poisoning in a mental hospital where, out of 38 patients in one ward, 6 developed symptoms. The author describes the bacteriological investigations undertaken and the finding of *Staphylococcus aureus* of the same phage type in the faeces of 5 out of 6 patients. The same phage type was isolated from the nose of the chef who prepared the food. The author concludes that a trifle prepared by hand by the chef on the previous day, and kept at atmospheric temperature for 24 hours before it was eaten, was the cause of the illness, though none of the food was available for bacteriological examination.

R. H. Parry

1686. **Notes on an Outbreak of Pemphigus Neonatorum in a Private Nursing Home**

G. C. WILLIAMS, C. SIMS-ROBERTS, and G. T. COOK. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* [*Mon. Bull. Min. Hlth*] **6**, 13–20, Jan., 1947. 10 refs.

A nursing home, well situated, with 20 beds all in large, well-ventilated, single rooms, but with only one labour ward, one sterilizing room, a small nursery, no milk kitchen, and no separation unit, was the scene of the outbreak of pemphigus neonatorum. The bookings were limited and the average stay in the home was 14 days. The staff was adequate.

In the discussion the authors refer to a number of points of interest revealed by the investigation. Each patient had her own private practitioner in attendance and " the list of doctors was a formidable one ". There was no scheme whereby the staff could be made aware of any abnormal circumstances in connexion with the different cases in the home, and each practitioner had his or her own ideas about the management of cases. General conditions in the home were excellent. Sufficient evidence was found to account for spread; for example, there was no dry-sterilization of masks and there were no facilities for drying napkins or for " dry-sweeping " the floors. Although the lesions were mild the results of swabbing showed a wide distribution of *Staphylococcus aureus* in the community. Bacteriophage typing was of great value in detecting the " epidemic strain ".

R. H. Parry

1687. **Quaternary Ammonium Compounds as Preservatives for Milk.**

C. K. JOHNS and H. V. PRITCHARD. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **37**, 500–504, Dec., 1946. 6 refs.

It has been claimed in Canada that solutions of quaternary ammonium compounds make better agents for cleansing dairy utensils than hypochlorites because they are less sensitive to organic matter. The authors of the present paper examined four proprietary articles for their action in preserving milk, though their addition to milk would be illegal in Canada as it is in Britain. The articles tested were " emulsept ", " roccal ", " hyamine 1622 ", and r-2-L. They were tested at strengths of 560 parts per million, 150 p.p.m., 100 p.p.m., and 70 p.p.m. against formaldehyde at 25 and 250 p.p.m. These concentrations were used because they were the strongest which could not be detected in the milk by taste. Samples were incubated for 18 hours at 60° F., as were two untreated control samples. The plate count was determined and the methylene blue and resazurin tests performed. In the first series the quart bottle of milk to be tested was mixed by repeated inversion, but in spite of this the controls, which consisted of the first and last sample, gave such different results that it was assumed that the cream had not been properly dispersed. In four subsequent tests the milk was poured backwards and forwards from one quart bottle to another. This gave more uniform results. Some discrepancies appeared in the resazurin test owing to the reducing action of formaldehyde on resazurin, and to a lesser extent on methylene blue, over and above the reducing action of the bacteria present.

The general conclusion reached was that each of the quaternary ammonium compounds tested exerted a slight but definite bacteriostatic action when added to milk in the highest concentration which might hope to escape detection by taste. Nevertheless, their value was extremely limited, for in no instance was the preservative effect remotely comparable to that exercised by formaldehyde. Emulsept, with the highest concentration, was least effective in inhibiting bacterial growth.

[It was unfortunate that these agents were tested against formaldehyde and not against hypochlorite which is the most commonly used sterilizing agent in Britain; also that the composition in chemical formulae of the proprietary articles tested was not given.]

W. A. Lethem

1688. **Emergency Sterilization of Drinking Water with Heteropolar Cationic Antiseptics. II. Persistence of Germicidal Action within Intestinal Tract and Removal of Excess Drug with Adsorbing Agents**

F. J. MOORE and J. MARMORSTON. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **26**, 729–732, Sept., 1946. 3 refs.

Heteropolar cationic antiseptics have a relatively low acute oral toxicity and are relatively free from inactivation by high concentrations of organic nitrogenous materials and alkalinity. Possible objections to the use of these chemicals are: (*a*) that their action may be reversed in the intestinal tract; and that (*b*) the slight taste and unknown risk of chronic toxicity make it desirable to remove excess chemical after antisepsis is complete.

Tests were made with 1 in 10,000 and 1 in 20,000 dilutions of " zephiran " against a turbid suspension of *Salmonella enteritidis* in sterile water. These suspensions were fed to mice and unsterilized suspensions to

controls. All the controls died. All the mice receiving 1 in 10,000 suspensions of zephiran survived; only one of those receiving a 1 in 20,000 suspension died. No reversal of action, therefore, occurred within the intestines of mice. Further experiments showed that these chemicals, which are effective against Gram-negative bacteria and amoebic cysts, can be removed from solution in a biologically inert state by adsorption on colloidal clays.

[Heteropolar cationic antiseptics are surface agents in which the active portion of the molecule is the cation. Kessel and Moore in the first report on this investigation (*Amer. J. trop. Med.*, 1946, **26**, 345) stated that a large number of these antiseptics were found sufficiently effective *in vitro* against bacteria and cysts of *E. histolytica* to justify considering their use for the emergency sterilization of drinking water.] *C. O. Stallybrass*

1689. **Epidemiology Today**
F. M. BURNET. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 825–830, Dec. 14, 1946.

In the first part of this paper the author describes recent contributions to epidemiology made by Australian workers: Gregg's work on the relation between German measles sustained in early pregnancy and congenital defects in the offspring; the first recognition of two important rickettsial diseases—murine typhus and "Q" fever, the latter a more widespread and important disease than at first supposed; the investigation of herpes in the Hall Institute, Melbourne; and the work on psittacosis and tick typhus. He next discusses the control of common and minor infections; makes a cogent plea for "pure" science ("it is one of the joys of work in the medical sciences that there is hardly anywhere a problem in 'pure' science whose solution may not provide some new approach to a practical human need"); pays a well deserved compliment to Pickles, suggesting that his example might be followed by other general practitioners; and advocates the extension of the method of using human volunteers in the study of minor infections. Discussing epidemiological problems arising from human action he quotes as an example the incidence of jaundice in American troops immunized against yellow fever, the trouble being traced to the use of serum from donors unwittingly infected with the virus of one type of infective jaundice. Another example is the increase of drug-resistant strains of streptococci when sulphadiazine is used prophylactically. Finally, the author refers to epidemiology as an aspect of human oecology; [this is an excellent demonstration of the epidemiological bearing of the apostle's saying—"for we are members one of another"]. Three objects of study are suggested—the part played by genetic factors, the age incidence of infectious disease, and the part played by infectious disease in human history. He suggests that while historical writers have dwelt upon dramatic diseases—for instance, plague—they have neglected infant mortality. Down to the middle of the nineteenth century infant mortality was the main check on population growth. "It becomes a simple matter of arithmetic to realize that if infectious disease amongst unenlightened peoples is to be reduced to Western European levels, then the other two checks, famine and war, must come in its place. Quite seriously, I think that the major political happenings of the next hundred years will be determined by the relative speeds with which, on the one hand, preventible infectious disease is eliminated, and, on the other, knowledge of means of population restriction is made generally available."

[Perhaps this dichotomy is a little too simple, but all will agree with the author that, in spite of past discoveries, "there is still an inexhaustible field for useful work".] *M. Greenwood*

1690. **The Stillbirth-rate in England and Wales in Relation to Social Influences**
I. SUTHERLAND. *Lancet* [*Lancet*] **2**, 953–956, Dec. 28, 1946. 7 refs.

Between 1929 and 1940 the stillbirth rate for England and Wales decreased only 5% and deaths per 1,000 live births at ages under 4 weeks decreased 10%, while the death rate at ages 9 to 12 months decreased 48%. The author makes a regional comparison for 1929–40; the London boroughs had the lowest and Wales (all types of area) the highest rates. Only in Scotland is a statement of the supposed cause of stillbirth required on the certificate. The return for 1943 assigned 33% to difficulties in labour and accidental haemorrhage and 19% to "ill-defined and unknown causes". The stillbirth rate for a constant age is highest in nulliparae but begins to rise again after the first birth; there is a steady increase with age for all degrees of parity. As, however, there has been a considerable decrease in the stillbirth rate, especially since the war—in Wales the rate fell by 34% and in England by 27% between 1938 and 1944—factors of social-economic order must also be involved. During the war the environment of pregnant women deteriorated in many respects, but the stillbirth rate fell. Two social-economic factors, however, improved—nutrition and antenatal care. A test of this explanation is to see how well the stillbirth rate can be expressed in terms of other social-economic indices by means of a regression equation. The author used five, the crude birth rate, the proportion of occupied males over 14 in social classes iv and v, mortality rate of 3 to 12 months, number of persons per room in private families, and the percentage of occupied males out of work. The data related to the pre-war period. The result was, in the more favourable case (the county boroughs of England and Wales), to improve the accuracy of the estimate by about 30%. [If all we know is the mean stillbirth rate for a set of county boroughs, the best estimate we can give for each is the mean of all; but if we know the values of the five indices for each borough we should substitute a different estimate in each instance, unless, of course, the values of the indices were the same; the result would be that the square root of the average of squared deviations of predicted from observed in the second case would be about 30% smaller than in the first.] In other words, the indices chosen did not cover more than a moderate proportion of the factors of the stillbirth rate. *M. Greenwood*

INDUSTRIAL MEDICINE

1691. Historical Relationship of Mining, Silicosis, and Rock Removal

T. HOLMAN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **4**, 1–29, Jan., 1947. 35 figs., 13 refs.

This is a review of the development of present-day rock-drilling practice and its bearing on the production of silicosis among miners. The author mentions briefly the methods of rock removal in use from the earliest days up to the eighteenth century, and indicates that silicosis incidence has increased *pari passu* with the speeding up of rock-breaking methods. Thackrah of Leeds in 1832 advocated measures, such as periodic examination of miners, which even to-day are being but tardily adopted. Barham in 1871 wrote that between the ages of 45 and 65 years the death rate in Cornwall was nearly three times as high among miners as among the rest of the population, and the deaths from pulmonary disease, at age 15 years or over, were almost twice as high in Cornwall as in the rest of England. Rock removal was at this time done mainly with the hand drill—held by one man while the striking was done by two others with sledge-hammers; " fire-setting " (heating of the rock face by fire and subsequent pouring of cold water upon it) and the use of " plug-and-feather " wedges were still in vogue. The hand drill was a relatively slow and inefficient method of boring, and dust risk was correspondingly lower than in recent times. In the same way black-powder blasting, though a real cause of dust, was not nearly so productive of it as modern explosive, which shatters the rock more completely.

Machine drills appeared about 1850, and early types were used in driving the Mont Cenis tunnel; they suffered from over-complexity of design, and the fact that steel at that time would not stand up to the work of drilling rock at high speeds. Those drills produced much dust, but not as much as the more efficient drilling patterns which followed them, and the dispersal of this dust into the air was almost totally disregarded until the turn of this century, all drilling at this time being done " dry ". Ogle in 1892 stated that mortality from phthisis among Cornish miners was from 5 to 6 times as great as among fishermen. The use of jets of water directed at the hole being drilled was probably first tried in driving the St. Gothard tunnel. In the Cornish mines water was first used by simply pouring it from a tin into the drill-hole; later, sprays were attached to the drill. Between 1851 and 1891 170,000 miners emigrated from Cornwall and worked overseas, mainly in the South African gold-fields, where the new rapid drilling methods were in use entirely without dust control; the length of active life of a miner about 1900 is stated to have been as little as 5 years; blasting was done at any time in the shift, and ore was shovelled dry.

Reference is made to J. G. Leyner, whose experimental work resulted in the modern rock-drill, and the early piston drill is contrasted with the hammer drills in use to-day. The first type was designed to blow a current of air down a channel in the drill steel in order to clear the hole of stone chips and dust. Miners soon declined to use this drill because of the dust produced, and Leyner adopted the plan of passing water as well as air down the drill-steel channel. On the expiration of Leyner's patent rights in 1913 water-feed drills became universally used in metal mining.

The advance of dust-preventive legislation in South Africa is detailed and the type classification of silicosis there adopted is described. A valuable graph showing silicosis incidence in the period 1918–35 is given. Dust concentrations on the Rand in 1902 were as high as 424 mg. per cubic metre at the face; since 1924 the average dust concentration in the mines has been 1 mg. or less. This reduction of dust has been accompanied by a lowering of silicosis incidence, an amelioration of the prevalent form of the disease, and an increased exposure time before it develops. Reference is made to the use of aluminium prophylaxis and the layout in use in Canada is described. Information on foam-wetting, diamond-drills, venting of drills, hardened-steel bits, dust-educators, and mist-projectors is given, and their effect on dust production indicated.

[An outstanding feature of this paper is the great number of excellent illustrations included. The quoting of average figures for a whole mine is unsound, as it may tend to mask the presence of a few highly dusty places, and these may produce much disease.]

L. W. Hale

1692. Byssinosis in the Cotton Trade

C. I. C. GILL. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **4**, 48–55, Jan., 1947. 7 refs.

The author reviews the scanty literature on byssinosis, which is a respiratory disease caused by the inhalation of cotton dust. Cotton from all countries of origin may give rise to this condition. When received at the factory in bales cotton is much contaminated by particles of sand and soil, leaves and seed. The bales have to be broken up and cleaned of dust by mechanical means and currents of air. The compressed cotton must also be mixed so that appropriate long and short fibres are mixed together. The machines which do this work become choked with fibre and dust, and those tending them are exposed to much dust and need special clothing and respirators. Dust-proof covers are fitted to all machines when possible. When the cotton reaches the stage in which it is to be worked up into long strands it leaves the blowing room and enters the carding room, where the operatives in charge of these machines are most affected. Each engine is cleaned 4 times a day by a vacuum machine and twice weekly has to be brush-stripped. It was noted that operatives, more in the past than to-day, experienced a dry, irritative feeling in the throat and chest when starting the week's work. This was known as Monday-morning fever or mill fever. Sometimes an attack of sneezing occurred, and in women particularly there was often a transient urticarial rash on the forearms. Mild conjunctivitis might be present. After a few hours, or perhaps a day, the symptoms ceased for the rest of the week. Some operatives seem to develop an immunity, others never do. In some there is recurrence years after a free interval.

Symptoms may re-appear, usually in carding-machine workers 10 or 20 years after the original attacks. Cough becomes more severe, with some sputum, easy fatigue, and the persistence of symptoms into the middle and end of the week. Nocturnal attacks of an asthmatic character may occur, and in time the operative is unfit for work in middle life and even unfit for alternative work. There are no physical signs in the early stages of the disease, but later those of chronic bronchitis and emphysema are manifest. Vital capacity progressively diminishes. Apart from increased bronchial shadows *x*-ray examination shows the ordinary changes of this condition. To substantiate an appeal for compensation there must be proof of at least 20 years' exposure.

The dust responsible for the lesions is not mineral but consists of extremely fine particles of vegetable matter with no lower limit to size. It is thought that irritating soluble protein from these may penetrate the alveolar tissue, with the development of super-sensitivity in some employees. It seems unlikely that the late stage described can develop without the preparatory early stage of mill fever and a long period of cough. Modern carding machines are totally enclosed and improved methods of dust extraction used. If factories are not too crowded the dust is diluted; air conditioning is desirable. Operatives should be examined before being employed and those with an allergic history, mouth breathers, and others with nasal abnormalities should be excluded. Chest expansion should be adequate.

G. C. Pether

1693. **Study of Absenteeism during a Five-month Period Following Influenza " A " and " B " Vaccination**
M. N. NEWQUIST and R. C. PAGE. *Industrial Medicine* [*Industr. Med.*] **15**, 676–677, Dec., 1946. 1 ref.

A mild influenza epidemic which swept New York late in December, 1945, was associated with the type B influenza virus. Mass vaccination of 665 office employees (who voluntarily agreed to the test) with A and B influenza vaccine was thereafter carried out and absenteeism recorded for 5 months. This group lost 673 days from work (1·01 days per employee). A control group of 656 office employees (those who did not volunteer) lost 456 days (0·69 days per employee).

Donald Stewart

1694. **Studies in Occupational Morbidity (I)**
W. T. RUSSELL, G. P. B. WHITWELL, and J. A. RYLE. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **4**, 56–61, Jan., 1947. 3 refs.

Recognition of influence of occupations on health is not new, but accurate information was fragmentary until Farr's researches and until the Registrar-General (1921–3 and 1930–2), published Occupational Mortality Supplements which included, for the first time on a national scale, a comparison between the mortality of husbands and wives. The occupation followed at the time of death is not necessarily the one that had the greatest influence on the worker's mortality; he may have changed his occupation several times, hence the attempt, here recorded, to collect data as to occupational morbidity. The importance of such studies is illustrated by the fact that in an average pre-war year 26,000,000 working weeks were lost, while the cost in sickness payment was £18,000,000. The national need for maximum production requires new emphasis on occupational morbidity. The data examined were based on sickness absenteeism amongst 2,681 males and 717 females employed by a certain firm during 1944. Groupings were made as between workers engaged in " non-production " and " production ", but excluding staff and clerical categories. The production group consisted of assemblers, welders, labourers, and inspectors. The non-production, or " auxiliary ", services included police, fire brigade, cleansing department, transport, and electrical and machine maintenance. In the non-production group were included the elderly or unfit, who were, however, subject also to adverse health factors in the conditions of their work, such as change of shift, week-end work, and long hours, with off-duty times which were inconvenient for transport facilities and therefore made for fatigue. " Production " workers averaged 48 hours per week, with regular work which was interesting and often well paid. A relatively large amount of uncertified sickness occurred because many employees were " old retainers " and the management accepted their word for sickness as reason for absence. This inquiry confirmed the theory of Bashford, made in relation to General Post Office workers, that some have a " sickness-proneness " due more commonly to psychoneurosis but in a few cases to " social irresponsibility ", like the classical case of the man who " came all over giddy " at the sight of a job of work. The following are the conclusions:

1. Although the occurrence of certified illness was relatively more frequent amongst women than amongst men in the production departments, its average duration was approximately 7 days shorter.

2. The percentage of possible time lost on account of certified sickness was lower for women than for men in both the production and the non-production shops, but their rates for uncertified illness were greater.

3. There is evidence to indicate, amongst both men and women, that in the case of certified illness there were some workers who had a " sickness-proneness " due either to chronic or recurring physical disabilities or to social irresponsibility. It is reasonable to suppose that " sickness-proneness " will also occur in the uncertified group.

4. The rates of uncertified illness in the industry under review are high and suggest the need for a reconsideration of policy in respect of certification requirements. This would be in the interests of the worker and the employer, and would help future investigations of occupational morbidity and its causes.

5. The sickness absence form (Report No. 85) devised by the Industrial Health Research Board has greatly improved the value of the records now being put at our disposal for future use, as it has helped to avoid some of the defects inherent in the data on which the present analysis was based.

[The relative smallness of the numbers weakens the force of statistical deductions though not perhaps of the

general inferences, including the need for further studies on these lines. The authors themselves emphasize further defects: (1) the amount of sickness that was uncertified, (2) the relative inaccuracies in medical certificates from the standpoint of a scientific inquiry. For these reasons they call their inquiry a " pilot study ".]

J. Greenwood Wilson

1695. **Better Use of Laboratory Procedures For More Accurate Diagnosis in Industrial Medicine**

W. C. Dreessen and R. F. Sievers. *Industrial Medicine* [*Industr. Med.*] **15**, 621–626, Nov., 1946. 16 refs.

Laboratory tests are of importance as an aid in diagnosis of disease, but their value should not be over emphasized, and they should not be allowed to replace physical examination and the investigation of occupational and medical history. The physician must know the limitations and facilities of the laboratories in his area, and must realize that the procedures involved in his requests often require such elaborate equipment and technical knowledge that the ordinary clinical laboratory cannot possibly provide reliable results. Three types of test are discussed: (1) specific tests which determine quantitatively the amount of a toxic agent present in biological fluids or materials; (2) tests which measure a metabolic or conjugated product of the toxic agent; and (3) tests which measure physiological disturbances or detect structural changes in organs and tissues. These are presented in three comprehensive tables which show at a glance the normal levels of toxic agents or their metabolic products in the biological materials used for analysis, and the upper limit of safe absorption or figures indicating abnormal absorption. The author condemns routine demands for tests on a " hit-or-miss " basis in the hope of an early diagnosis and appeals to industrial physicians to make proper use of laboratory procedures.

A. Lloyd Potter

1696. **The Control and Elimination of Silicosis in the West Coast Haematite Iron Ore Industry**

J. Craw. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **4**, 30–47, Jan., 1947. 18 figs., 9 refs.

The author gives a concise history of events up to 1935, when the Silicosis Act came into being for the haematite iron ore mining industry. In 1934, when he was appointed medical director to a large mining company in West Cumberland, he laid the foundation of a long-term investigation into the significance and magnitude of the problem of pneumoconiosis. As regards silicosis incidence, the haematite iron ore is of two types, (1) compact, hard, brownish-red or purple to bluish-grey ore—the predominating type in the Egremont district; and (2) soft, dull, reddish-purple ore in the Hodbarrow mines and Furness district. The hardness of the ore determines the type and use of pneumatic drills and quantity of explosives, which in turn is related to the amount of dust produced. Chemical analysis of the ore shows that insoluble residues vary from 7 to 20% and that the washed residue shows a large preponderance of quartz, with a small amount of amorphous silicate of alumina and an almost infinitesimal amount of silicate of iron. Radiologically haematite possesses 4·5 times the radiological density of coal dust, and this fact must be borne in mind when reading radiographs of an iron-ore miner's chest. The *x*-ray changes are classified as (1) exaggerated linear markings, (2) radiological reticulations, (3) radiological nodulation, and (4) massive shadows.

It is demonstrated that in reticulation, which is the most difficult problem, the changes are almost always due to the simple accumulation of inspired dust in the alveoli and in the lymphatic channels and that there is no evidence of mature fibrous tissue. The pathological anatomy of conglomerate fibrosis is similar to that of the massive fibrosis seen in all silicosis due to mixed dusts. At necropsy 75% of these cases show evidence of tuberculous infection. A group of 191 men from the Egremont district, who had spent their entire working life in the mines, were examined radiologically and classified. The incidence of radiological change increased with the number of years underground, until in men over 40 years old only 1 in 10 had a normal chest, and 70% showed massive changes. Reticulation *per se* did not cause alteration in tolerance to exercise or in total lung volume, and was not incapacitating. A similar group of men from the Furness district, where the ore is softer and more easily worked, showed no evidence of massive shadows and no reticulation. Only 5 cases had evidence of reticulation, but all had also spent some years in American copper mines. The difference in findings from the two districts supports the accepted theory that the noxious action of a dust is directly proportionate to the particulate size.

Since 1935 in these districts control has been exerted from both mining and medical angles. A mist projector is used, and oil is introduced into the spray to make a sticky film on the dropped dust and prevent its being disturbed after settling. The mist projector is kept in action for 10 to 15 minutes after the shot firer has exploded his charge, to ensure that the working place is atmospherically clear. The dust content of the air has thus been reduced from 4,000,000 to 5,000,000 per ml. to about 2,500 per ml., giving approximately 250 particles of silica per ml. Medical control consists of (1) pre-employment examination and selection of men intermediate between the pyknicosomatic and the leptosomatic types; (2) radiological examination of the chest; and (3) periodic complete examination during the working life of the miner. Sixty-six men have been followed up accurately during 8 to 10 years underground, and in them there is no evidence of any radiological change in the lungs. The author describes this as 100% success. The results of 68 necropsies on haematite miners suffering from silicosis in the past 10 years are tabulated, and it is shown that tuberculosis is an important lethal factor in haematite fibrosis and silicosis. It is suggested that infection, usually tuberculous, is the single incapacitating and death-causing factor and that silicosis will cease to be a problem if the incidence of tuberculosis is strictly controlled and eradicated.

A. Lloyd Potter

Genetics

1697. **The Inheritance of Cleidocranial Dysostosis**
G. W. LASKER. *Human Biology* [*Hum. Biol.*] **18**, 103–126, May, 1946. Genealogical charts, 270 refs.

This rare developmental disease affects especially those bones which ossify from membrane. The most prominent feature is defect or absence of the clavicles with unusual mobility of the shoulder girdle. The head is typically large, with persistent fontanelles and sutures, and the facial bones and teeth are poorly developed. Dwarfism, spinal curvature, spina bifida, and defects of the lower limbs are frequent. The paper reviews 505 cases now known, and 30 doubtful ones. The majority of families reveal dominant inheritance, with no more than 5 or 6 instances of the skipping of a generation. There is one marked peculiarity in transmission, however: affected men tend to transmit the gene to their sons and affected women to their daughters. Furthermore, affected sons of affected mothers tend to transmit the gene more often to their daughters than to their sons, and conversely for affected sons of affected fathers. This is also true of affected women. These findings cannot be explained on any known genetic basis. Seventy cases are isolated, with no affected relatives. They may be due directly to mutation or else there is an alternative mode of causation, dependent on a dominant gene. Recessive inheritance is not involved. *J. A. Fraser Roberts*

1698. **The Genetic Theory of Schizophrenia. An Analysis of 691 Schizophrenic Twin Index Families**
F. J. KALLMANN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **103**, 309–322, Nov., 1946. 18 figs., 15 refs.

The twin material was systematically collected on a State-wide basis in New York. The chance of developing schizophrenia by the age of 45 was 0·85% in the general population of the State. Among the relatives of the twin index cases the frequencies were as follows: marriage partners, 2·1%; parents, 9·2%; half-sibs, 7%; full sibs, 14·3%; fraternal co-twins, 14·7%; identical co-twins, 85·8%. The raised frequency in marriage partners is attributed to mate selection. The other frequencies show a steady increase as blood relationship to the schizophrenic index case becomes closer. In 5·7% of instances the parents were blood relatives. While identical twins are 6 times more like each other than are fraternal twins in regard to morbidity, when extent, course, and outcome are studied the identical twins are 55 times more like each other than the fraternal twins. Thus the factors which make for resistance to the disease process appear to be strongly hereditary. The author advances the hypothesis of a single recessive factor determining morbidity and multifactorial inheritance of susceptibility to the established disease. He does not rule out the possibility that these are identifiable, in which event inheritance of schizophrenia as a whole might be multifactorial. It is stressed that genetic influences are not the sole cause, as is shown by the 14·2% of discordant identical twins. Psychological theories of a descriptive or analytical nature are not invalidated, nor is the psychiatric belief that schizophrenia can be prevented. *J. A. Fraser Roberts*

1699. **Inheritance of Anomalies of Teeth and Jaws in Relation to Constitution.** (Über die Vererbung von Gebiss- und Kieferanomalien sowie ihren Zusammenhang mit der Konstitution)
J. GÁSPÁR and A. G. KOCSIS. *Zeitschrift für Stomatologie* [*Z. Stomatol.*] **43**, 341–355, Aug., 1946. 18 figs., 10 refs.

The authors present 2 families in which prognathia was inherited as a " strongly dominant " character; 3 members of each family were actually examined. It is claimed that prognathia is part of the asthenic constitution; but even this small material contains some asthenics without prognathia and, what is probably more important, there is one pyknic with that anomaly. [Without denying that the relation postulated by the authors may exist, the argument seems somewhat unconvincing on the evidence presented.] *H. Grüneberg*

1700. **Microspermia in an Individual from a Family of Unusually High Sex Ratio and Low Fertility**
H. HARRIS. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **13**, 156–159, Aug., 1946. 3 figs., 4 refs.

The author suggests that the traits mentioned in the title of the paper may be genetically connected.
H. Grüneberg

1701. **The Inheritance of Premature Baldness in Men**
H. HARRIS. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **13**, 172–181, Nov., 1946. 9 refs.

Out of a series of 900 normal men between 30 and 42 years of age, 120 were found to be prematurely bald. A family study was carried out. It is concluded that premature baldness and late baldness are genetically distinct, and that premature baldness behaves as a Mendelian dominant gene which is rarely manifested in women. *J. A. Fraser Roberts*

1702. **A Contribution to the Genetics of Hair Colour in Man**
C. D. LEE and L. S. PENROSE. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **13**, 182–183, Nov., 1946. 1 ref.

A method is described of measuring the concentration of chromogen in human hair. This provides an objective quantitative character which may prove useful in genetic and racial studies. *J. A. Fraser Roberts*

Physiology and Biochemistry

1703. **Ultra-violet Absorption in Living and Dead Cells**
E. M. BRUMBERG and L. T. LARIONOW. *Nature* [*Nature, Lond.*] **158**, 663–664, Nov. 9, 1946. 1 fig., 3 refs.

Tissue cultures of mouse mammary carcinoma and mouse and chicken fibroblasts were photographed in ultraviolet light of wave lengths of 254 to 275 $\mu\mu$, using visible light for the preliminary focusing. In contrast with Caspersson's findings, the nuclei failed to absorb these wave lengths except for moderate absorption by the nucleoli. Cancer-cell cytoplasm absorbed moderately. After injury of the cells by exposure to ultraviolet light, by hypertonic solutions or mechanically, the nuclei absorbed ultraviolet light as described by Caspersson, whose results are attributed to the use of cells injured by the preliminary focusing in ultraviolet light. Apparently uninjured living cells contain a somewhat altered form of ribonucleic acid which does not absorb ultraviolet light of a wave length of about 260 $\mu\mu$.
L. Foulds

1704. **Presence of Rubidium in Animals.** (Sur la présence générale du rubidium chez les animaux)
G. BERTRAND and D. BERTRAND. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **72**, 805–809, Sept.–Oct., 1946. 9 refs.

By analytical and spectrographic methods the authors have already shown rubidium to occur in minute quantities in many types of plant. As much as several centigrammes per kilo of dry tissue may occur (*Ann. Inst. Pasteur*, 1946, **72**, 416). A number of workers have by spectrographic methods detected minute quantities of rubidium in animal tissues—in human and cows' milk, human blood, hens' eggs, and the whole bodies of worms. Quantitative observations were very approximate, and some of the observations may be regarded as doubtful. The authors have analysed tissues for rubidium after low-temperature ashing in 13 invertebrates and 23 vertebrates. Most of the invertebrates were analysed whole, but any shells were removed and the faeces also. In the vertebrates different organs were analysed. In the invertebrates the values obtained lay between 3 and 28 mg. per kilo of dry tissue with one exception—*Ascidia mentula*, where it was 45·5 mg. In the 6 estimations on cold-blooded vertebrates the values lay between 2 and 20·5 mg. The 11 estimations on mammals lay between 8 and 65·5 mg.; the 6 on birds were mostly from pectoral muscle and all gave over 100 mg. These high levels may have some connexion with the activity of the tissue and certainly with its relative radioactivity.

From this small series it would appear that rubidium occurs widely in animal tissues as well as in plants, and must be classed among the elements found in all living matter.
R. E. Rewell

1705. **Biological Incorporation of a Choline Homologue into Liver Phospholipids**
C. S. MCARTHUR. *Science* [*Science*] **104**, 222–223, Sept. 6, 1946. 6 refs.

The author reports experiments on rats which were given daily doses of an unnatural lipotrope, tri-ethyl-β-hydroxyethyl ammonium chloride, and the resultant recovery of triethylamine from the liver phospholipids. It is claimed that these observations support the view that choline exerts its lipotropic effect through favouring the synthesis of lecithin. The contrast between the results obtained and those of Channon *et al.* (*Biochem. J.*, 1937, **31**, 2181) is attributed to the use of larger doses, a longer experimental period, and different fractionating procedures. Full details of this work will be published shortly.
A. C. Frazer

CIRCULATION

1706. **The Validity of Internal Jugular Venous Blood in Studies of Cerebral Metabolism and Blood Flow in Man**
E. B. FERRIS, G. L. ENGEL, C. D. STEVENS, and M. LOGAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **147**, 517–521, Nov. 1, 1946. 5 figs., 8 refs.

It has often been assumed that blood taken from the internal jugular vein is representative of mixed cerebral venous blood. This assumption takes no account of the intercommunication which has been shown to exist between the cerebral, cranial, and extracranial venous circulations through the plexuses of the skull, and the consequent possibility that the blood in the two internal jugular veins may differ significantly owing to anatomical differences between these plexuses on the two sides. The presence of these intercommunications introduces the further complication that hyperventilation may vitiate the results of blood analysis, for hyperventilation decreases cerebral blood flow but increases extracranial blood flow. Any inaccuracy due to anatomical differences between the two sides would thus be exaggerated, the two internal jugulars carrying a different proportion of extracranial blood. The authors' experiments show that in fact significant differences occur between the two sides, and that the method of estimating cerebral blood flow by means of clearance of inert gases from jugular blood is subject to inaccuracy.
Raymond Greene

1707. **The Conducting System of the Vertebrate Heart**
F. DAVIES and E. T. B. FRANCIS. *Biological Reviews* [*Biol. Rev.*] **21**, 173–188, Oct., 1946. 182 refs.

A brief review is given of the most important work on the structures responsible for the initiation and conduction of the impulse to contraction in the vertebrate heart. The authors conclude that in fish, amphibia, and reptiles

the cardiac muscle fibres form a continuum with the same general histological characters in all parts of the heart. They point out that since there is no structural specificity of the muscle fibres factors other than purely morphological ones must account for the different intrinsic rhythms displayed by the individual heart chambers. They suggest, on the basis of unpublished work, that a differential distribution between auricle and ventricle of certain chemical substances (glycogen, phosphocreatine, and adenosine compounds), known to be concerned with muscular contraction, may have a bearing on this problem.

In birds and mammals, specialized tissue (the nodes, A-V bundle, and Purkinje fibres) has been developed to initiate and conduct the impulse to contraction. The structure and distribution of these specialized fibres are in general the same for birds and mammals. There are, however, certain differences which the authors hold may be related to the different functional requirements of the hearts. Collateral evidence is brought to support the view that the specialized tissues of the avian and mammalian heart are not remnants of more extensive tissues of a similar nature in lower vertebrate hearts, but are new developments associated with the more rapid heart rate in the higher vertebrates.

R. T. Grant

1708. **The Reaction of the Vessels of the Mesentery and Intestine to Angiotonin and Renin**
R. G. Abell and I. H. Page. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 166–169, Aug., 1946. 4 figs., 11 refs.

The mesenteric and intestinal vessels of 4 rabbits were observed through a microscope. In order to do this a portion of the intestine had been permanently herniated into a transparent chamber in the manner described by Zintel (*Anat. Rec.*, 1936, **66**, 437). The animals were observed 1 to 14 days after the exteriorization of a portion of the intestine. Renin (0·1 to 0·4 ml.) prepared by the method of Helmer and Page (*J. biol. Chem.*, 1939, **127**, 757) or angiotonin (0·2 to 0·5 ml.) prepared by the method of Page and Helmer (*J. exp. Med.*, 1940, **71**, 29) was injected into a lateral ear vein. Both substances caused vigorous peristalsis of the intestine and constriction of the arteries and veins of the mesentery and arteries of the intestine. Neither substance caused constriction of the capillaries nor, according to the authors, any appreciable change in the rate of the mesenteric blood flow. These findings are in accord with the action of renin and angiotonin on the somatic vessels.

H. E. Holling

1709. **Acceleration of Thrombin Formation by a Plasma Component**
P. Fantl and M. Nance. *Nature* [*Nature, Lond.*] **158**, 708–709, Nov. 16, 1946. 1 fig., 5 refs.

According to Quick, prothrombin has 2 components combined with calcium, but this view is contested. The authors prepared a pure prothrombin by adsorption on to barium carbonate and elution. Thrombin was prepared from this prothrombin by incubating with a thromboplastin (brain extract or Russell viper venom) and calcium ions; the thrombin was then added to a purified fibrinogen preparation in the *p*H range 6·0 to 7·2. The reaction rate of thrombin formation is slow, but the kinetics of the reaction fit in with results to be expected only if prothrombin is the sole precursor of thrombin. No evidence supporting a complex structure of prothrombin isolated from human plasma was obtained. It was, however, found possible to accelerate the rate of thrombin formation by using, instead of purified fibrinogen, a plasma from which prothrombin had been completely removed by adsorption. This result suggests that normal plasma coagulation depends not only on the presence of adequate prothrombin but also on the presence of an accelerator which is separate from prothrombin and fibrinogen.

M. C. G. Israëls

1710. **Coagulation of Preserved Plasma.** (La coagulation du plasma conservé)
P. Fredericq. *Bulletin de la Société de Chimie Biologique* [*Bull. Soc. chim. biol.*] **28**, 540–542, July–Sept., 1946. 6 refs.

Pyocyano-coagulase, a proteolytic enzyme extracted from cultures of *Ps. pyocyanea*, will clot in 10 minutes oxalated rabbit plasma which has been stored in the ice chest for 1 month, as opposed to the 3 hours required for clotting of fresh oxalated plasma under the same conditions. This is due to an acceleration of the activation of prothrombin to thrombin, since pyocyano-coagulase produces a considerable quantity of thrombin from the stored oxalated plasma in 30 minutes, but no appreciable amount from fresh plasma in 3 hours. The stored plasma therefore retains its prothrombin; as it cannot be reactivated by addition of calcium alone or of calcium and lipoids, neither of these can be the direct activator of prothrombin. The activator would appear to be the plasma tryptase, the proteolytic activity of which seems to be lost on storage. The fresh plasma contains also a labile antitryptase whose disappearance in stored plasma accounts for the more rapid activation of prothrombin by pyocyano-coagulase and for the more rapid fibrinolysis it brings about after clotting. Other tryptic enzymes activating prothrombin are prodigioso-coagulase (from *Bacillus prodigiosus*) and actinomyceto-coagulase (from *Actinomyces albus*). Staphylo-coagulase acts equally well in fresh and stored plasma by direct conversion of fibrinogen to fibrin.

T. R. Parsons

1711. **Platelet Counts and Platelet Function**
P. M. Aggeler, J. Howard, and S. P. Lucia. *Blood* [*Blood*] **1**, 472–496, Nov., 1946. 18 figs., 31 refs.

This paper gives an account of an investigation undertaken to determine the significance of reductions in the platelet count in terms of established normal standards, and to discover what relations exist between the platelet count, the bleeding time, the coagulation time, clot retraction, and capillary fragility. These determinations

were made in 64 normal subjects and in 404 patients suffering from various diseases. Platelet counts were carried out by the Rees and Ecker method. Clot retraction was measured by the method of Aggeler, Lucia, and Hamlin, and was expressed as the fluid volume of the clot. The Ivy method was employed for the bleeding time, and the Dalldorf negative-pressure method was used to determine capillary fragilities. Coagulation times were measured by the method of Lee and White. The values for the normal platelet count were: mean, 409,000 per c.mm.; standard deviation, 68,000 per c.mm.; normal range, 273,000 to 545,000 per c.mm. Normal values for the fluid volume of the clot were: mean, 7·9%; standard deviation, 6·0%; normal range −4·1% to 19·9%. The normal values for the bleeding time were: mean, 3·2 minutes; standard deviation, 1·6 minutes; normal range, 0 to 6·4 minutes. There were 10 or fewer petechiae in 92% of the normal subjects studied, and this value was accepted as normal. The normal values for the coagulation time were: mean, 8·9 minutes; standard deviation, 2·7 minutes; normal range, 3·5 to 14·3 minutes. The distribution of these results carried out on 64 normal subjects and on the 404 patients are given in 10 histograms.

Tests were carried out on 23 cases of primary thrombocytopenic purpura. The platelet counts during the active phases in all but 2 patients varied between 30,000 and 190,000 per c.mm. Within this range there appeared to be no significant correlation between the level of the platelet count and the severity of the bleeding. In these cases the bleeding time was prolonged in every instance; in 21 of the 23 observations it was longer than 30 minutes. Clot retraction was markedly diminished in all cases, and in 18 cases the capillary fragility was increased. The prothrombin level was slightly reduced in 4 cases. In 2 cases there was a significant prolongation of the coagulation time. The same tests were carried out on 28 cases of secondary thrombocytopenic purpura. In these the platelet counts varied between 20,000 and 24,000 per c.mm. The bleeding time was prolonged in 18 of these cases, moderately prolonged in 7, and slightly prolonged in 1. The capillary fragility was markedly increased in 11 cases. Clot retraction was diminished in 25 cases, the coagulation time was prolonged in only 2 cases, and the prothrombin level was diminished in 12 instances.

Nineteen cases of secondary thrombocytopenia without bleeding were similarly investigated. The average of the platelet counts was 210,000 per c.mm., as compared with 100,000 per c.mm. in primary thrombocytopenic purpura and 140,000 per c.mm. in secondary thrombocytopenic purpura. The bleeding time was noticeably prolonged in 2 cases, moderately prolonged in 5, slightly prolonged in 2, and normal in 10. Clot retraction was diminished in 8 cases and normal in 11. Capillary fragility was much increased in 6 cases, slightly increased in 2, and normal in 11. The prothrombin concentration was diminished in 4 cases and normal in 15. The coagulation time was normal in all cases. Fifteen cases of thrombocytopenia complicating other haemorrhagic conditions showed an average platelet count of 225,000 per c.mm. The bleeding time was markedly prolonged in 3 cases, moderately prolonged in 2, slightly prolonged in 2, and normal in 8. Clot retraction was diminished in 7 cases and normal in 8. Capillary fragility was increased in 6 cases and normal in 9. The prothrombin concentration was reduced in 8 cases and normal in 7. The coagulation time was markedly prolonged in 2 patients, both of whom suffered from haemophilia.

There was a statistically significant relation between the platelet count and the results of tests of clot retraction, bleeding time, and capillary fragility, but there was no significant relation between the platelet count and the coagulation time. Factors other than platelet count or platelet function which may influence the results of these tests are discussed. The critical level of the platelet count below which abnormal bleeding is likely to occur was found to be 190,000 per c.mm. in primary thrombocytopenic purpura and 230,000 per c.mm. in secondary thrombocytopenic purpura. Counts as low as 100,000 per c.mm. were, however, found without abnormal bleeding, and as high as 280,000 per c.mm. associated with a prolonged bleeding time. In all patients in the bleeding stage of primary thrombocytopenic purpura, and in most with secondary thrombocytopenic purpura, the bleeding time was much prolonged and clot retraction was significantly diminished. In one-half of the patients showing thrombocytopenia without bleeding or with thrombocytopenia associated with other haemorrhagic diseases the results of the tests were abnormal. In some patients during the stage of recovery from thrombocytopenic purpura the platelet counts became normal, but bleeding time, clot retraction, and capillary fragility remained abnormal. In others these measurements became normal long before the platelet count. These results are interpreted as representing variation in the functional capacity of the platelets.

R. Winston Evans

RESPIRATION

1712. **Decline in the Rates of Sweating of Men working in Severe Heat**

S. D. GERKING and S. ROBINSON. *American Journal of Physiology* [*Amer. J. Physiol.*] **147**, 370–378, Oct., 1946. 1 fig., 3 refs.

It appears from this paper that the mechanism of sweating is subject to fatigue. The experiment was carried out on men well acclimatized to heat who were walking on a treadmill at a high temperature for periods of 6 hours. The men retained their water balance by drinking saline. The average rate of sweating in the first 2 hours was 1,400 g. per hour; the rate declined thereafter by from 10 to 80% by the sixth hour. The decline depended on environment. It was greater in humid atmospheres, when the initial rate was high, and when the men wore clothes.

Raymond Greene

1713. **The Ferricyanide Method of Blood-Analysis**

F. C. COURTICE and C. G. DOUGLAS. *Journal of Physiology* [*J. Physiol.*] **105**, 345–356, Jan. 15, 1947. 3 figs., 17 refs.

1714. **Studies on Positive Pressure Respiration. I. General Aspects and Types of Pressure Breathing. II. Effects on Respiration and Circulation at Sea Level**
A. L. BARACH, M. ECKMAN, E. GINSBURG, C. C. RUMSEY, I. KORR, I. ECKMAN, and G. BESSON. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **17**, 290–320 and 356, Aug., 1946. 3 figs., 9 refs.

This paper records studies in the problems of pressure breathing carried out at the Aviation Research Laboratory of Columbia University, New York, from 1941 to 1944. A comparison was made of three methods of raising the intrapulmonary gas pressure to increase the arterial oxygen saturation, so as to enable aviators to function efficiently at altitudes between 38,500 and 46,000 ft. (11,500 and 14,000 m.) without using a pressurized cabin or suit. The methods tried were mask alone, mask plus pressurized waistcoat, and mask plus pressurized waistcoat and pants to relieve the muscular stress of expiration against the increased intrapulmonary pressure. To compare these three methods a series of tests were employed as follows:

(i) Assessment of pulmonary ventilation and tidal air volume by means of a 9-litre spirometer with a high-speed motor blower inserted into the breathing circuit to give the required positive pressure.
(ii) Measurement of the transverse diameter of the chest, at the level of the ninth dorsal vertebra, by *x*-ray photograph taken at a distance of 6 ft. (182 cm.).
(iii) Estimation of the peripheral and central venous pressures in relation to breathing oxygen at 12 and 20 cm. of water above atmospheric pressure. The peripheral venous pressure was assessed by puncturing the antecubital vein with a gauge 19 needle connected by rubber tubing to a manometer and a reservoir filled with normal saline; the central venous pressure was measured by passing a fine catheter through one antecubital vein into the right auricle, its position being checked by fluoroscopy.
(iv) Recording of pulse rate, pulse volume, and arterial blood pressures by the usual digital and sphygmomanometric methods; also by direct measurement of the pressure in the femoral artery by means of a Hamilton manometer.
(v) Estimation of the arm-to-tongue circulation time after injecting intravenously 3 ml. of 20% sodium decholinate.
(vi) Observation of the cardiac output by means of the ballisto-cardiograph and by estimating the oxygen content of samples of blood collected under oil from the right heart and femoral artery simultaneously, at half-hour intervals, while breathing room air, 100% oxygen without pressure, 100% oxygen at 20 cm. water pressure, and room air, in that order.
(vii) Assessment of haemoconcentration in blood samples collected half an hour after positive pulmonary pressure was applied, by estimating the oxygen capacity and the plasma protein of the blood.
(viii) Measuring the transverse diameter of the heart by exposing films for 1 second so as to include diastolic volume, while breathing at a positive pressure of 20 cm. of water.

Briefly, these experiments showed that, although the mask alone can be used to raise the intrapulmonary pressure by 20 cm. of water, the addition of external equalizing pressure over thorax and abdomen by means of a pressurized waistcoat and pants results in more comfortable breathing, less interference with cardiac output and the return of venous blood to the heart, a smaller increase in the residual air, and far less haemoconcentration.

[These results confirm the findings of pilots and physiologists in England who used these methods of pressure breathing operationally with considerable success in 1944 and 1945—the Bazett pressure waistcoat plus the Gilson mask was much preferred to the Gagge mask alone.] *H. E. Whittingham*

NUTRITION

1715. **The Determination of the Nitrogen Balance Index in Normal and Hypoproteinemic Dogs**
J. B. ALLISON, J. A. ANDERSON, and R. D. SEELEY. *Annals of the New York Academy of Sciences* [*Ann. N.Y. Acad. Sci.*] **47**, 245–271, Oct., 1946. 9 figs., 23 refs.

1716. **The Evaluation of Protein Quality in the Normal Animal**
R. H. BARNES and D. K. BOSSHARDT. *Annals of the New York Academy of Sciences* [*Ann. N.Y. Acad. Sci.*] **47**, 273–296, Oct., 1946. 8 figs., 24 refs.

1717. **The Electrophoretic Studies on the Effect of Protein Depletion on Plasma Proteins and the Regeneration of Plasma Proteins after Oral Administration of Hydrolysates prepared from Casein and Lactalbumin**
B. F. CHOW. *Annals of the New York Academy of Sciences* [*Ann. N.Y. Acad. Sci.*] **47**, 297–316, Oct., 1946. 3 figs., 31 refs.

1718. **Blood Protein Regeneration and Interrelation**
G. H. WHIPPLE, F. S. ROBSCHEIT-ROBBINS, and L. L. MILLER. *Annals of the New York Academy of Sciences* [*Ann. N.Y. Acad. Sci.*] **47**, 317–326, Oct., 1946. 5 refs.

Haemoglobin and globulin injected parenterally into dogs are utilized for formation of haemoglobin and plasma protein. Plasma proteins injected in the same manner are used completely. The effect of protein in forming haemoglobin is greater than that of haemoglobin. Digested haemoglobin is as effective as whole haemoglobin in maintaining nitrogen balance, but gives rise to more undetermined nitrogen in the urine. The pigment moiety of haemoglobin injected intraperitoneally is excreted. The efficiency of haemoglobin for restoring body protein is increased by addition of *dl*-methionine but not by *dl*-isoleucine. A mixture of ten essential amino-acids given by mouth or parenterally is well utilized; there is no evidence that the unnatural isomers are toxic. The amino-acid mixtures can be given rapidly in 10% solution and cause less clinical disturbance than do any digested proteins. Glutamic acid by vein may cause vomiting. Maximal output of the haemoglobin is nearly 1 g. per kilo body weight per day. Maximum formation of plasma protein cannot be reached by this technique. *J. R. Marrack*

1719. **Diet and Canine Hysteria. Experimental Production by Treated Flour**
E. MELLANBY. *British Medical Journal* [*Brit. med. J.*] **2**, 885–887, Dec. 14, 1946. 6 refs.

Canine hysteria has been recognized for some 30 years, and many guesses have been made about its aetiology. Of late, food has been considered the most likely causal agent, particularly dog biscuit, though there has been

disagreement as to whether the toxic action of an unknown substance or some untraced specific deficiency is the most likely exciting cause. The disease has often occurred among the dogs kept at the author's laboratory, where outbreaks of it have been associated with the eating of bread from certain sources. Records have been kept of the particular samples of bread which have been associated with the appearance of hysterical fits, and a miller has confirmed the author's suspicion that the samples of bread which produced fits were all made from flours which had been heavily bleached and probably improved. It seemed likely that nitrogen trichloride was the offending bleaching and improving agent; feeding tests were therefore carried out in which dogs were given bread made from two kinds of flour, both derived from the same grist, 1 treated with nitrogen trichloride and the other untreated. Fits were never seen in dogs fed on the untreated material, while the treated flour was associated with the appearance of fits after periods of feeding which varied between 1 and 4 weeks. Dogs differed in susceptibility, and not all those eating the treated bread developed hysteria. However, the fits could always be stopped by changing to a variety made from untreated flour, and dogs showing no symptoms of hysteria while eating untreated bread often showed symptoms soon after they began to eat treated bread. Animals which had been eating the treated bread for long periods might take a long time to behave in an entirely normal way, though their actual attacks of hysteria stopped quickly after changing the diet. The mode of action of the bleaching agent has not been explained. It seems possible that nitrogen trichloride acts on certain amino-acids of the proteins of wheat gluten, and experiments to test this point are being made. In the meantime it is of some interest to recall the fact that a large proportion—possibly 90%—of the flour milled in this country and destined for human consumption is at present "agenized"—that is, treated with nitrogen trichloride.

S. J. Cowell

1720. **Gastric Emptying and Intestinal Absorption of Dextrose Solutions**

E. F. BIRCHALL, P. F. FENTON, and H. B. PIERCE. *American Journal of Physiology* [*Amer. J. Physiol.*] **146**, 610–612, July 1, 1946. 11 refs.

This is a study of the rate of emptying of the stomach and absorption from the intestine of dextrose solutions of various concentrations and volumes. The dextrose solutions were fed to young mature female rats, and the contents of the stomach and of the intestines were analysed separately. In most cases sugar did not enter the large intestine. The amount of dextrose emptied from the stomach was greater with large volumes of dilute dextrose solutions than with small volumes of concentrated solutions, the amount of dextrose fed being constant. The rate of absorption was somewhat greater from the more concentrated solutions of small volume. Emptying and absorption were greater with large than with small volumes of identical concentration, and were greater with concentrated than with dilute solutions of identical volume.

K. Black

1721. **Research Work on Iron Metabolism by means of a Radio-active Iron Isotope.** (Recherches sur le métabolisme du fer à l'aide d'un isotope radioactif de fer)

A. VANNOTTI. *Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften* [*Bull. schweiz. Akad. med. Wiss.*] **2**, 90–97, Oct., 1946. 2 figs.

Radioactive iron, Fe^{52}, was given intravenously to rabbits as citrate and lactate in ferrous and ferric forms. A few hours after injection Fe^{52} was detected in nearly all the organs. After 3 days the amount in the red blood cells rose, and after the tenth day it had disappeared temporarily from the plasma, but the amount in the red cells continued to accumulate and special tests demonstrated its presence in the haemoglobin molecule. With large doses, 2 to 3 mg., a big proportion was excreted by the kidneys even during the first half hour, but at first only a little appeared in the bile. Fe^{52} continued to accumulate in the haemoglobin, reaching a maximum at the fourth week, and about this time the amounts in the bone marrow, spleen, and muscles began to rise rapidly; excretion by bile also began to increase. This increase, which was accompanied by corresponding increase in plasma iron, is attributed to the breakdown of the red cells. Deposition of Fe^{52} in the liver occurs within $1\frac{1}{2}$ hours of the injection. The liver is considered to be the chief storage depot and the regulator of exchanges of iron with other parts of the body. Ferrous and ferric Fe^{52} show some differences. The red cells take up radioactive iron more rapidly in ferric than in ferrous form; ferric Fe^{52} is excreted sooner than ferrous, especially in the early stages, and ferric Fe^{52} also leads to more rapid deposition in the liver. In anaemic as compared with normal rabbits the red cells, the liver, the bone marrow, and muscles, especially of the heart, take up Fe^{52} much more quickly and excrete less in the urine and bile. Damage to the liver by phosphorus causes Fe^{52}, which had accumulated in the liver, to decrease rapidly.

H. E. Magee

1722. **Glucose Ingestion during Severe Anoxia**

L. VAN MIDDLESWORTH. *American Journal of Physiology* [*Amer. J. Physiol.*] **146**, 491–495, July 1, 1946. 2 figs., 19 refs.

Male rats weighing 150 to 200 g. were exposed to a barometric pressure of 258 mm. Hg in glass chambers. After 4 hours at that pressure they were quickly returned to normal pressure and given glucose by stomach tube, 5 ml. of a 10% solution per 100 g. body weight. The pressure was then restored to 258 mm. Hg, and groups of 10 animals were removed from the chambers at 30-minute intervals for blood-sugar estimation. Urine samples were obtained, keeping the rats at the low pressure for further periods of 2 or 3 hours. The stock diet was high in carbohydrates. Animals fasted for 12 hours before an experiment, and were not used for more than one experimental series to avoid the possibility of acclimatization. Prolonged hyperglycaemia and glycosuria were found; the blood sugar (average of 46 cases) reached 171 mg. per 100 ml. 1 hour after the ingestion of glucose, 192 mg. at 2 hours, and at 3 hours

began to fall. In spite of the high blood sugar, the glycogen content of liver and heart was less than that found in controls at sea-level pressure. The blood sugar of 10 control rats kept at sea-level pressure was 133 mg. per 100 ml. 1 hour after glucose, and had returned to normal at 1½ hours. *K. Black*

1723. **Vitamin B and Fat Anabolism**
Nature [*Nature, Lond.*] **158**, 349–350, Sept. 7, 1946.

This article is a short review of work done mainly by McHenry and his co-workers in Toronto. On a high-carbohydrate low-fat diet rats do not lay down fat unless vitamin B_1 is present. The amount laid down in the presence of this vitamin is increased if other components of the vitamin B group are present. The type of fat is different from that deposited on a normal diet and is affected by the various components of the vitamin B group. It is possible that the effect of vitamin B_1 is brought about through pyruvate, in the metabolism of which it is known to participate, and acetaldehyde (a probable intermediary of fat metabolism). The synthesis of fat from protein requires vitamin B_1 and pyridoxine. This effect of the vitamins of the B group in fat synthesis may influence our conception of the essential nature of the unsaturated fatty acids. It now seems possible that in the original experiments, in which these acids were shown to be dietary essentials, the amounts of these vitamins may have been inadequate, and that if the vitamins were given in optimal quantities the animal might be able to synthesize these unsaturated fatty acids. *J. Yudkin*

1724. **Absence of Rapid Deterioration in Moderately Active Young Men on a Restricted Intake by B-complex Vitamins and Animal Protein**
R. C. Cogswell, G. H. Berryman, C. R. Henderson, C. W. Denko, and J. R. Spinella. *American Journal of Physiology* [*Amer. J. Physiol.*] **147**, 39–48, Sept., 1946. 4 figs., 16 refs.

Seven healthy young men were kept under observation for 12 weeks, during which time they received a controlled diet of about 3,200 calories containing 70 g. of protein and a sufficiency of the individual members of the vitamin B complex such as would be expected in a diet containing plenty of foods rich in protein of animal origin. The men were subjected to a series of physical and psychomotor tests at regular intervals in order to obtain some measure of their efficiency in certain directions. The urine and faeces were collected throughout the whole of the experiment for chemical analysis. After the preliminary period most of the foods rich in animal protein were removed from the diet, which then, for 5 weeks, contained only 48 g. of protein (94% of it being of vegetable origin), and anything between one-half and one-sixth of the previous quantities of the various individual B vitamins. The efficiency tests during this second period showed no clear indication of any falling off in the level of performance brought about by the change of diet. There was a pronounced drop in the urinary excretion of B vitamins during the second period, but the faeces contained greater quantities of most of the B vitamins than during the control period of greater intake. The average daily faecal output respectively of thiamine, riboflavin, and nicotinic acid was equal to, or larger than, the daily intake of these substances throughout the period of restricted diet. *S. J. Cowell*

1725. **The Liberation of Aneurin, Cocarboxylase, Riboflavin, and Nicotinic Acid from Autolysing Yeast Cells**
K. T. H. Farrer. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **24**, 213–217, Sept., 1946. 6 figs., 13 refs.

Brewer's yeast was autolysed at the optimum temperature of 50° to 52° C. After a latent period preceding autolysis, the liberation of aneurin, riboflavin, and nicotinic acid was a linear function of time and was complete in less than 2½ hours. Preliminary cold storage shortened both the latent period and the time required for complete liberation of the vitamins. Cocarboxylase is hydrolysed to free aneurin during autolysis. The aneurin is not affected by continuation of the hydrolysis up to 24 hours. *J. Yudkin*

1726. **The Effect of Salicylates and Thiamine Deficiency on the Thiamine Content of Rat Tissue**
J. B. Cleland. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **24**, 227–230, Sept., 1946. 18 refs.

Administration of salicylates increased the liver weight per g. body weight and the thiamine concentration in the liver of adult (but not young) rats on both normal and thiamine-deficient diets. Thiamine concentration in kidney and brain, kidney weight, and the rate of development of symptoms of thiamine deficiency in young rats were not altered by administration of salicylates. In young thiamine-deficient rats the thiamine concentration in brain was lower than in adult deficient rats, but the concentrations in kidney and liver were much the same; on a normal diet the concentrations in kidney and brain were similar in adult and young rats, but the thiamine concentration in the liver was significantly higher in adult rats. *J. Yudkin*

1727. **Changes in the Concentrations of Carotene and of Vitamin A in the Blood of Sheep Grazing on Natural Pastures in South Australia**
A. W. Peirce. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **24**, 231–240, Sept., 1946. 1 fig., 21 refs.

The concentration of vitamin A in the blood of Merino sheep which grazed on natural pasture was found to lie between 25 and 35 μg. per 100 ml. plasma. The concentration was not affected by changes in the intake of carotene from 1 mg. while the sheep were grazing on dry pasture in the autumn to 2 g. per day while they were grazing on green pasture in the spring. There was, however, a slight but significant increase in the concentration of vitamin A in the blood with age. Carotene was present in the blood in measurable amounts only

when the sheep were grazing on green pasture. The amounts at such times, however, were only 5 to 15 μg. per 100 ml. plasma, or 10 to 20% of the total vitamin-A potency of the blood. In an area where perennial bush (*Kochia sedifolia*) formed the major constituent of the diet the concentration of vitamin A in the blood was found to lie within the normal limits, except at the end of a period of 2 years in which the rainfall was below normal. At this time the concentration had fallen to about two-thirds of the normal value. In all the sheep examined the reserves of vitamin A in the liver were adequate; they ranged from 230 to 810 μg. per g. liver. Carotene was present to the extent of only 2 to 5 μg. per g. liver. *J. Yudkin*

1728. **Deterioration on Storage of Dried Skim Milk**
K. M. Henry, S. K. Kon, C. H. Lea, J. A. B. Smith, and J. C. D. White. *Nature* [*Nature, Lond.*] **158**, 348–349, Sept. 7, 1946. 18 refs.

Samples of milk of a moisture content of 3, 5, and 7·6% were stored in air or in nitrogen at temperatures of 37°, 28·5°, and 20° C. They were analysed at intervals, and details of the changes after 60 days are shown. Many changes are recorded, including decreased palatability and solubility and an increased acidity. Special stress, however, is laid on the changes in the protein which showed a lowering of the biological value, a decrease in the free amino-acid groups, and an increase in the amount of reducing sugar bound to protein. The decrease in amino-nitrogen did not occur in stored pure milk protein unless reducing sugar was present. The authors suggest that at least part of these changes occur as a result of a Maillard reaction between the aldehyde groups of reducing sugar and the free amino-groups. These consist largely of ε amino-groups of lysine, and the amount of this amino-acid is in fact decreased during storage. The deleterious effects of storage are far greater when the moisture content is higher, and also when the temperature is higher. On the other hand the replacement of air by nitrogen makes little difference to the rate of deterioration. *J. Yudkin*

ENDOCRINES

1729. **The Relationship of the Parathyroid Glands to the Action of Estrogen on Bone**
B. L. Baker and J. H. Leek. *American Journal of Physiology* [*Amer. J. Physiol.*] **147**, 522–526, Nov. 1, 1946. 4 figs., 13 refs.

Large doses of oestrogen administered to young rats cause increased density in trabeculation in the subepiphysial region of some long bones. The suggestion that this is caused by the parathyroid and pituitary glands was examined. Groups of intact and parathyroidectomized female rats, 32 to 90 days old, were given 20 daily subcutaneous injections of either 250 μg alpha-oestradiol in 0·05 ml. peanut oil or 0·05 ml. peanut oil alone. At necropsy the tibiae were examined, the mean thickness of the epiphysial cartilage was measured, and the mean number of cells per row and the number of hypertrophied cells were counted.

A decrease in thickness of the epiphysial cartilage was found in both groups of oestrogen-treated rats (0·187 and 0·205 mm. compared with 0·304 mm. in intact and parathyroidectomized controls). This is probably due to decreased proliferation of cartilage cells, as the mean number of these cells per row decreased from the control values of 21·1 and 20 to 13·1 and 14·7 in the intact and parathyroidectomized groups respectively. The number of hypertrophied cells in the intact rats was 3·9 and 3·2 as against 3 and 3·2 in the parathyroidectomized rats. In both groups of oestrogen-treated animals the dense trabecular region was much more extensive than in the control groups. The tests were carried out on 2 groups of 12 intact rats and on 10 control and 14 oestrogen-treated parathyroidectomized rats. No animal was included in the parathyroidectomized group if evidence of parathyroid tissue was found on microscopical examination. These experiments do not explain the mechanism involved in this action of oestrogen on bone, but they show that there is no need to postulate the participation of the parathyroid glands, because the same effect can be produced in their absence.

S. A. Simpson

1730. **On the Action of Adrenaline on the Blood Vessels in Human Skeletal Muscle**
W. J. Allen, H. Barcroft, and O. G. Edholm. *Journal of Physiology* [*J. Physiol.*] **105**, 255–267, Dec. 6, 1946. 11 figs., 23 refs.

The transience of the vasodilatation that occurs with intravenous infusion of adrenaline has been described incidentally by other workers; the authors of this paper examine the phenomenon in detail. Records were taken of the blood flow in the limb (forearm or calf), of the heart rate, and of the arterial blood pressure during both intravenous and intra-arterial infusion of adrenaline. Infusion of adrenaline at the rate of 10 μg. per minute into the antecubital vein resulted in a fourfold to fivefold increase in the blood flow through the forearm for the first 2 minutes; it then fell to twice the resting level, and remained constant at that rate until the end of the infusion; the heart rate showed the same qualitative changes, sometimes a short time before the blood-flow changes. The increase in the blood flow could not have been a passive vascular effect, as there was very little change in the mean arterial pressure, and also the infusion of adrenaline at the rate of 1 μg. per minute, which was too small to have any significant effect on the heart rate, did increase the blood flow in the forearm. Similar blood-flow changes occurred when adrenaline was infused into sympathectomized forearms, hence vasomotor reflexes were not implicated. When adrenaline was infused into the femoral artery at a rate of 2 to 3 μg. per minute the blood flow in the calf was increased 5 to 6 times, but there was no change in either heart rate or blood pressure; there was, however, a small but delayed increase in the blood flow in the forearm. The authors conclude that the effect of the adrenaline is due to its action in the limb,

and, specifically, in the skeletal muscle, as the changes in blood flow through the hand, which has relatively little muscle in comparison with the forearm, were small.

In their discussion the authors reject the hypothesis that the fall after the initial great rise was due to cutaneous vasoconstriction, as the fall is itself greater than the initial flow through the whole forearm, skin, and muscle. Other workers have shown that in animals adrenaline causes dilatation of the capillaries followed by constriction of the arterioles; the suggestion is that this also occurs in human skeletal muscle. *W. S. S. Ladell*

REPRODUCTION

1731. **The Relation of Temperature and the Thyroid to Mammalian Reproductive Physiology**

R. BOGART and D. T. MAYER. *American Journal of Physiology* [*Amer. J. Physiol.*] **147**, 320–328, Oct., 1946. 6 figs., 13 refs.

Reproduction is affected principally by two external factors—light (birds and some mammals) and temperature (fishes). In the latter a rise in temperature stimulates the gonads, whereas in rams a condition of "summer sterility" is produced by periods of high temperature. Determinations during the period July 5 to Sept. 13 in 4 normal rams showed a decline in the number of spermatozoa per ejaculate from 1,678,810,000 to 335,400,000, in semen volume from 2·03 to 0·23 ml., and an increase in abnormal spermatozoa from 39 to 90%. Histological examination showed a complete absence of spermatogenesis.

The present investigation confirms the work of Berliner and Warbritton that high temperatures act indirectly through the thyroid by affecting the rate of thyroxine secretion. Daily subcutaneous injections of either 1 g. of crystalline thyroxine (3 animals) or 1 g. of iodized casein (5 animals) during the period of "summer sterility" restored fertility to some extent. Values for the number of spermatozoa per ejaculate, semen volume and proportion of abnormal spermatozoa in the pre-treatment period (July 5 to Aug. 2) and during the period when treatment was given (Aug. 2 to Sept. 13) were respectively 822,190,000 and 1,501,563,000; 1·34 and 0·50 ml.; and 37 and 29%. Oral administration was also effective. One ram receiving 1 g. of iodized casein daily (material containing approximately 2% of *dl*-thyroxine) showed an increase in sperm motility from 1+ to 5+, in percentage of live spermatozoa from 10 to 85, and a fall in abnormal spermatozoa from 83 to 15%. It was mated with 5 ewes; 3 became pregnant and delivered 5 lambs. A condition closely resembling "summer sterility" was produced during the autumn breeding season by thiouracil administration. Daily injection of 2·5 g. of thiouracil (1 animal) caused a reduction in semen volume from 0·3 to 0–0·1 ml., in number of spermatozoa per ejaculate from 618,000,000 to 16,000,000, in motility from 3 to 1, and an increase of abnormal spermatozoa from 39 to 90%. The histological picture closely resembled that in rams with summer sterility. Oral administration of 10 g. of thiouracil was less effective. The values for semen volume, number of spermatozoa, motility, and proportion of abnormal spermatozoa being respectively 0·35 to 0·30 ml.; 1,121,000,000 to 500,000,000; 3 to 1; 24 to 65%. There was a complete absence of spermatozoa in the lumen of the seminiferous tubules.

That these results were due to the reduction of thyroxine secretion and not to the toxic action of thiouracil was shown by feeding 2 or 4 g. thyroactive protein daily to a ram receiving injections of 2·5 g. of thiouracil. Values found during a pre-treatment period and during the addition of 2 and 4 g. of thyroactive protein were: semen volume 0·6, 0·3, and 0·5 ml.;—number of spermatozoa per ejaculate—1,374,000,000, 578,000,000, and 1,397,000,000; motility—2, 0, and 1+; abnormal spermatozoa—36, 86, and 64%. The results showed that the thyroactive protein, particularly in doses of 4 g., was able to counteract the effect of thiouracil. *S. A. Simpson*

1732. **Studies on the Metabolism of Semen. 3. Fructose as a normal constituent of seminal plasma. Site of formation and function of fructose in semen**

T. MANN. *Biochemical Journal* [*Biochem. J.*] **40**, 481–491, 1946. 48 refs.

The reducing sugar in semen is shown by optical activity, reducing value, and formation of methylphenylfructosazone, to be *d*(–)-fructose. This, as shown by colorimetric determinations made by Roe (*J. biol. Chem.*, 1934, **107**, 15) and Stewart, Scarborough, and Davidson (*Quart. J. med.*, 1938, **7**, 229), may be present to as much as about 1% in the semen of some species (bull): in man the semen fructose amounts to 100 to 200 mg. per 100 ml., its concentration being, however, much less exactly regulated than that of the blood glucose. The fructose is added to the semen by the seminal vesicles or, in forms not possessing these organs, by the prostate, but not by the epididymis.

The fructose of the semen is metabolized to lactic acid by a hexokinase reaction with adenosine triphosphate in the spermatozoa, leading to the formation of fructose monophosphate, followed by further metabolism through fructose diphosphate, triose phosphate, glycerophosphoric acid, and pyruvic acid. The rate of fructolysis is much reduced at a temperature approaching 0° C. Glucose oxidase does not destroy any significant amount of the reducing sugar of the semen, which therefore cannot include glucose; but spermatozoa can metabolize to lactic acid added glucose or mannose, thereby sparing fructose. Normally, however, spermatozoa utilize fructose, as this is the chief sugar available in seminal plasma. *T. R. Parsons*

1733. **Efficacy of Protein Hydrolysate in the Restoration of Serum Protein in Hyperimmunized Horses after Blood Depletion**

P. N. BASU and S. N. SEN. *Journal of Hygiene* [*J. Hyg., Camb.*] **45**, 56–58, Jan., 1947. 1 fig., 7 refs.

Pharmacology and Therapeutics

1734. **Narcosis and the Precipitation of Cellular Lipoids.** (Narcose et précipitation des lipoides cellulaires)
M. Dodé, P. Gavaudan, and H. Poussel. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **223**, 521–523, Sept. 30, 1946. 3 refs.

There are certain analogies between the phenomena of cellular inhibition and the precipitation of benzene, from aqueous solution, by the addition of a third substance, soluble in both benzene and water. This suggests that anaesthesia by inert narcotics might be produced by precipitation of lipoids within the cell. It can be shown that such a precipitation would be consistent with the requirements of thermodynamic theory. The molecular composition of the precipitated substance is not influenced by that of the substance causing the precipitation; the action is governed by the relative solubilities of the lipoid and the precipitant in water and in each other. It is possible to calculate the minimum solubility of the precipitant for such a reaction. A substance with a lower solubility than this cannot be included among the inert precipitants. This precipitation obeys the theoretical requirements of anaesthesia with inert narcotics: alteration of thermodynamic activity in the intracellular solvent, a minimum solubility of the narcotizing agent, and a lower limit of thermodynamic activity below which an inert narcotic ceases to act. A theory of anaesthesia based on precipitation by the action of the narcotic drug is compatible with the requirements of thermodynamics. This reaction, it would seem, is actually a precipitation of complex lipo-proteins. *Ronald Woolmer*

1735. **Preliminary Conditions of a Theory of Narcosis Produced by Indifferent Narcotics.** (Conditions préliminaires d'une théorie de la narcose par les narcotiques indifférents)
P. Gavaudan, M. Dodé, and H. Poussel. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C. R. Acad. Sci., Paris*] **223**, 407–408, Sept. 2, 1946. 7 refs.

Chemically inert narcotics inhibit such diverse processes as irritability, cell division, and photosynthesis. These inhibitory effects are examples of the action of the narcotic on protoplasm in general—not on cell elements in particular. Thus, though the arrest of cell division may be a consequence of an alteration in the nucleus, this is in itself dependent on a more general cytoplasmic change which is the true cause of the phenomenon. Narcosis may be defined as the structural or functional modification of certain processes which occur in all types of cell and which are indispensable to its activity. No theory of anaesthetic action can be reliably based on the modification of any one kind of cellular activity. Though anaesthesia may be the main effect, it is often accompanied by modifications of the cell, such as changes in metabolism, permeability, water balance, and viscosity, and various theories based on these phenomena have been evolved. These complex phenomena are so closely interrelated, however, that it is inadmissible to single out any one and attribute a causal role to it.

Theories of lipoid action and adsorption are in a stronger position. They are based on quantitative relations, such as the constancy of the concentration of the anaesthetic agent in the lipoids during anaesthesia (Meyer and Hemmi), the constant value of thermodynamic activity of the anaesthetic agent (Ferguson), and the correspondence between narcotic potency and surface tension (Traube). To elaborate a theory of anaesthetic action in accordance with these relationships consideration must be given to the physical nature of the substrate on which the narcotic acts. It must be shown that a given reversible change is produced in the substrate by a narcotic with a certain thermodynamic activity, and that this action is independent of the nature of the anaesthetic agent. The anaesthetic agent should produce, by its mere presence, a constant modification of the cellular reactions whenever its thermodynamic activity attains a certain minimum value. A theory closely allied to the Meyer-Overton theory can be shown to fulfil these conditions. *Ronald Woolmer*

PENICILLIN

1736. **The Action of Penicillin Esters**
J. Ungar. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 606, Oct., 1946. 1 ref.

The guinea-pig, rat, and mouse are able to hydrolyse penicillin esters to free penicillin; the rabbit and man are not. Intramuscular injection of penicillin esters into mice therefore provides a depot from which penicillin is slowly liberated into the blood. Rabbits and men fed on large doses of penicillin esters showed no circulating penicillin; it is therefore improbable that penicillin esters will prolong the therapeutic effect of penicillin in man. *C. L. Oakley*

1737. **Turbidimetric Assay for Penicillin**
C. A. Green. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 559–564, Oct., 1946. 8 refs.

Dilutions of "unknown" solutions containing penicillin are made in phosphate buffer at *p*H 6·2, followed by dilution in glucose broth so as to contain between 0·4 and 2 units per ml. To each of 3 tubes is added 0·5 ml. of diluted unknown and 20 ml. of glucose broth seeded with the Oxford "H" strain of staphylococcus to give 5×10^6 organisms per ml. A standard rack is made up of quantities of a freshly made penicillin standard varying from 0 to 1 unit on an arithmetic scale,

plus 20 ml. of seeded broth in similar tubes. The tubes are incubated for about 4 hours, and the turbidity produced in the tubes containing the unknowns is compared with the turbidity curve of the standard tubes. The method is simple, and the results reproducible to about ±4%.

[A better standard calibration curve would be obtained by the use of a logarithmic scale of amounts of standard.]

C. L. Oakley

1738. **Penicillin Concentration in the Blood and Milk of Bovines**

G. SLAVIN. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **39**, 793–795, Oct., 1946. 1 fig.

Cows suffering from low-grade mastitis which had resisted penicillin treatment by direct injection into the udder were given from 114,000 to 128,000 units of sodium penicillin in aqueous solution intramuscularly every 3 hours for 24 hours. The highest blood level of penicillin recorded was 0·25 unit per ml., whereas in a normal cow a single injection (intramuscular) of 200,000 units of calcium penicillin caused a maximum blood level of 0·45 unit after 5 minutes, declining rapidly to 0·16 unit after 20 minutes, 0·1 unit after 40 minutes, and slowly to zero in 240 minutes. Similarly, 1 mega unit of penicillin in 4% beeswax–arachis oil given subcutaneously every 12 hours produced satisfactory blood levels. Indications are that 10 times the aqueous dosage is needed to produce the same blood levels of penicillin as those given by oily injections. Four tables of results based on groups of 4 or 5 cows give the concentrations of penicillin in the udder secretion from 48 to 144 hours after 2 administrations each of 100,000 units given as 50-ml.-volume injections through the teat canal. The conclusions reached are that this mode of treatment proved entirely successful in streptococcal mastitis, less successful in staphylococcal mastitis, and, despite normal sensitivity of the organism to penicillin, failed in *Corynebacterium pyogenes* infections of the udder. The methods of estimating penicillin were sensitive to 0·001 unit in blood and 0·031 unit in milk.

F. J. Dyer

1739. **Post-penicillin Jaundice**

R. R. HUGHES. *British Medical Journal* [*Brit. med. J.*] **2**, 685–688, Nov. 9, 1946. 11 refs.

In a military general hospital in India it was noted that of the cases admitted with alleged infective hepatitis 21% had had intramuscular penicillin treatment within the previous 2 to 7 months. Moreover, cases of jaundice were occurring in the penicillin research unit of the hospital. There was good *prima facie* evidence that jaundice was being transmitted from case to case through the syringe used for the penicillin injections. While it was not possible to check the technique of injection in those cases treated with penicillin before admission to the hospital, it was possible to check the technique employed in the hospital. Needles sterilized by heat were used, and a fresh needle was taken both for withdrawing the penicillin from the ampoule and for injecting the drug into the patient. The same syringe, however, was at times in use for several patients in succession.

In an experiment standard Army syringes with 19, 21, and 23 S.W.G. needles, after cleaning and sterilization, were charged with sterile normal saline. The saline was then injected intramuscularly (*a*) into muscles in a state of active contraction, and (*b*) into relaxed muscles. After injection of 1 ml. of saline the needle with the syringe attached was withdrawn, the needle was removed, and drops of saline exuding from the tip of the syringe were examined microscopically for red blood cells. It was found that contamination of the syringe with red blood cells had occurred in 15 of the 27 instances when the injection was made into a contracted muscle, and twice out of the 12 injections into a relaxed muscle. Experiments showed that there were three possible mechanisms which, either separately or together, might account for this contamination: (*a*) back-pressure forcing fluid from the muscle into the needle; (*b*) spread of blood from the tip of the needle towards the syringe; and (*c*) suction when removing the needle from the syringe.

[Once again it has been demonstrated from clinical practice and by experiments that for the avoidance of "syringe jaundice" not only needles but also syringes must be adequately sterilized after each single use.]

John F. Loutit

1740. **The Intestinal Absorption of Penicillin G**

V. P. SEEBERG, P. L. ILLG, and D. J. BROWN. *Science* [*Science*] **104**, 342–343, Oct. 11, 1946. 1 fig., 6 refs.

Experiments were performed on 44 cats under dial anaesthesia. Sodium penicillin II (G) 0·1 millimol per kilo of body weight was placed in the ligated duodenum and the amount left at various periods up to 3 hours determined: after 1, 2, and 3 hours, 76, 57, and 56% was recovered from the duodenum. When 0·1 millimol of sodium sulphadiazine per kilo was placed in the duodenum only 12% was recovered after half an hour and 5% after 1 hour. Hence penicillin, in contradistinction to many sulphonamides, is badly absorbed in the upper part of the intestine, and is probably destroyed by bacteria and inactivating enzymes in the lower part before complete absorption can take place. Efforts to increase the efficiency of oral penicillin should be directed towards increasing the penetration through the intestinal mucosa.

J. M. Robson

1741. **Inhibition of Various Clostridia by Penicillin in Human Serum**

R. W. N. L. ROSS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 441–447, July, 1946. 4 figs., 19 refs.

Concentrations of penicillin inhibitory to *Clostridium welchii* and one strain each of *Cl. oedematiens* and *Cl. septicum* were investigated. Since it has been shown that Brewer's medium containing sodium thioglycollate is not destructive of penicillin, tests were made first in liquid culture by means of series of dilutions of penicillin in this medium. Neutral red was used as an indicator, growth producing an intense greenish-yellow fluorescence

due to the marked drop in Eh which was produced. Concentration just permitting growth of 3 strains of *Cl. welchii* ranged from 0·1 to 0·8 unit per ml., with an average of 0·4 unit. Two other strains were inhibited by 0·06 unit per ml. The strains of *Cl. septicum* and *Cl. oedematiens* tested failed to grow in the presence of 0·2 unit. Concentrations permitting minimal growth produced abnormal morphology, particularly with one strain of *Cl. welchii* which grew as very long filamentous forms imperfectly divided by septa, giving rise in culture to an appearance like mould floating in a clear medium. On agar blocks containing penicillin morphological changes were observed in *Cl. septicum*, which lost its spores and became longer. Human serum with the addition of 1 : 500 sodium thioglycollate was used as a medium for the growth of clostridia in slide cells and capillary tubes. Penicillin titrations were carried out with *Cl. welchii* and with a staphylococcal control. Decreasing strengths of penicillin were diluted 1 : 10 with a mixture consisting of 500 parts of fresh serum treated with sodium thioglycollate and 25 parts of a 1 : 100 dilution of 24-hour culture of the clostridium in Brewer's medium. Effective concentrations were similar to those obtained in the tube test. The resistance of clostridia was found to be 2 to 30 times that of staphylococci, but partial inhibition and atypical morphology were induced in the most resistant strains at 10 times the concentration required for staphylococci.

The method was then applied to the investigation of the inhibitory concentration in the serum of individuals following single intramuscular doses of penicillin. Thioglycollate and culture were added to each sample of serum in the same proportions as in the titration experiment. The results of tests at different intervals after injection were compared with those of a similar test on the Oxford strain of *Staph. aureus*. It was found that doses of 100,000 per unit produce serum inhibition of growth of *Cl. welchii* for periods of 1½ to 3 hours. The highest dilutions tested (1 : 8) were effective after ½ to 1½ hours. Pure serum was effective in 2 of 3 cases for 2½ hours. Doses of 33,000 units were effective for 1 to 1½ hours, and 15,000 units for 1 hour. A somewhat more prolonged effect was produced upon the staphylococcal control. A dose of 100,000 units in 12 hours by continuous drip rendered the serum inhibitory for staphylococci only. The work of several investigators on the use of penicillin in prophylaxis and (sometimes associated with surgery, serum therapy, and sulphonamide therapy) in treatment has shown increasingly favourable results as dosage was raised. For example, with the use of 40,000 units 4-hourly or 20,000 units 2-hourly with sulphonamides the fatality rate was 11·5% in 96 cases; with irrigation (500 units per ml.) and 20,000 units 3-hourly intramuscularly (and amputation in several cases) 32 out of 33 cases recovered; with prophylaxis with 45,000 to 50,000 units 4- to 5-hourly or 20,000 units 3-hourly no deaths or amputations for gas gangrene occurred in 4,000 consecutive battle casualties. Though the author's *in vitro* tests appear to indicate a necessary dosage of about 10 times that for staphylococci, his serum concentration test in volunteers suggests a 100,000-unit dose as adequate for 1½ to 3 hours. *G. T. L. Archer*

1742. **Subcutaneous vs. Intramuscular Administration of Penicillin**

W. S. HOFFMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 1165–1169, Nov., 1946. 7 refs.

Intramuscular administration of penicillin has been preferred to subcutaneous injection because of the irritation and pain produced by the latter method. Symptoms depend to a large extent on the purity of the preparations used. Comparison was made with 3 preparations of penicillin: (1) an almost pure amorphous penicillin (1,550 units per mg.); (2) crystalline sodium penicillin (1,400 units per mg.); and (3) pure crystalline potassium penicillin (1,631 units per mg.). Under standard conditions the intramuscular and subcutaneous use of these preparations were compared. As regards pain, this was not found to be an important factor with any of the 3 solutions by either route, in contrast to the commercial preparations used in the same hospital. The subcutaneous route was slightly more comfortable as it involved the use of a smaller needle. Comparison of the penicillin levels in the blood showed that all 3 preparations gave essentially the same results in a total of 206 assays involving 618 estimations of the plasma penicillin level. No instances of urticaria or other form of sensitivity were seen. The authors conclude that the subcutaneous route is to be preferred for the administration of purified penicillin preparations.

Alan Kekwick

1743. **Allergic Dermatoses Complicating Penicillin Therapy**

G. H. BAUER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **54**, 292–299, Sept., 1946. 14 refs.

Toxic reactions following penicillin therapy in human beings are uncommon; those affecting the skin are considered under three headings: (1) urticaria; (2) the erythemato-vesicular group of reactions; and (3) contact dermatitis. Urticaria and the erythemato-vesicular group of reactions are seen only after administration of penicillin by injection, while contact dermatitis is seen only after external exposure.

Cases illustrating each group are described. Urticaria appeared on the ninth day and persisted for 6 days in a patient who was being given 15,000 units of penicillin intramuscularly every 4 hours. The author does not state whether the penicillin was still being given by the ninth day or whether it was discontinued when the rash appeared. Intradermal and patch tests with both commercial penicillin (10,000 units per ml.) and crystalline penicillin sodium G were negative. The erythemato-vesicular group of reactions occur within 24 hours of starting intramuscular administration of penicillin. The areas usually involved are the groins, hands, and feet, and this reaction is probably dependent on previous sensitization of the areas by some type of fungus infection, the reaction produced by the penicillin being of the nature of a dermatophytid eruption. Two cases are described in both of which there had been previous

attacks of dermatophytosis. It is of interest that in these 2 cases patch and intradermal tests with commercial penicillin were applied to the forearm and groins, and in each case the intradermal test in the groin was the only one which gave a positive reaction. Contact dermatitis occurs only after prolonged and heavy exposure to penicillin. The 2 cases reported were in male nursing orderlies. Patch and intradermal tests with commercial penicillin were positive in both cases, but tests with penicillin culture medium and crystalline penicillin sodium G were negative. *H. R. Vickers*

1744. **Anti-penicillin Action of Liver Extract.** (Action antipénicillinique d'un extrait de foie)
G. WERNER. *Compte Rendu des Séances de la Société de Physique et d'Histoire Naturelle de Genève* [*C.R. Soc. Phys. Hist. nat. Genève*] **63**, 65–68, April–July, 1946. 3 figs.

It is found that the antibiotic activity of penicillin is diminished proportionately by liver extract. Determinations were carried out on peptone broth cultures of *Staphylococcus aureus* incubated for 20 hours at 37° C. (with sodium penicillin and pure liver extract). This diminution of activity is due to the biotin, or vitamin H, of the extract. Activity was estimated by the curve of development of cultures of *Saccharomyces cerevisiae* in presence of biotin, which is depressed by increasing quantities of penicillin. These results are set out in graphs. Penicillin has no direct action on *Saccharomyces*, so there is probably a direct antagonism between penicillin and biotin.

In further experiments, 1 ml. of penicillin and 10 ml. of a standard peptone broth culture of *Staph. aureus* in each of a series of tubes were incubated for 42 hours at 37° C. with 0, 2, 4, 6, and 8 μg. of pure biotin. At the end the bacterial growth in each was estimated by its turbidity as compared with a standard tube containing culture but no biotin or penicillin. In the series the antibiotic action of penicillin is progressively overcome by the biotin, 6 μg. of penicillin being completely annulled by 8 μg. of biotin. Further investigations of this antagonism are in progress.

R. G. Bannerman

1745. **The Accuracy of Methods Employed for Titration of Penicillin.** (Étude de la précision des méthodes de titrage de la penicilline)
J. LESSIAU. *Annales d l'Institut Pasteur* [*Ann. Inst. Pasteur*] **72**, 835–839, Sept.–Oct., 1946.

The author compares three methods of estimating penicillin concentration (the Oxford method, Heatley's method, and Sureau's method) and considers the personal variation and the variation between repetitions of the same assay for each. He concludes that no figures for penicillin assay can be accepted unless the internal error of the method is less than 80%.

[Other observers claim better results than those recorded here.] *C. L. Oakley*

1746. **Filtrates of *Penicillium notatum* Cultures as Antidotes to Bacterial Toxins.** (Sur les propriétés antidotiques des filtrats de culture de " penicillium notatum " a l'égard des toxines microbiennes)
G. RAMON, R. RICHOU, and J. RAMON. *Presse Médicale* [*Presse méd.*] **54**, 637, Oct. 2, 1946. 17 refs.

Crude filtrates of cultures of *Penicillium notatum*, unlike pure penicillin, are able to destroy staphylococcal toxin and diphtheria toxin. Destruction is rapid at 37° C., slower at lower temperatures; heating filtrates to 55° C. does not abolish their capacity to destroy bacterial toxins; heating to 60° C. reduces it slightly. Addition of 0·5% commercial formol even with half an hour's heating to 55° C. does not reduce this capacity, and such formolized filtrates retain their activity for at least 3 months in the ice chest. Human serum slows the activity slightly but does not inhibit it completely. *C. L. Oakley*

1747. **Action of Penicillin in Preventing the Assimilation of Glutamic Acid by *Staphylococcus aureus***
E. F. GALE and E. S. TAYLOR. *Nature* [*Nature, Lond.*] **158**, 676–678, Nov. 9, 1946. 2 figs., 5 refs.

Many Gram-positive bacteria can concentrate glutamic acid from the media in which they are growing; since glutamic acid cannot pass through bacterial cell walls by simple diffusion, for this migration requires energy which must be supplied by bacterial metabolism, the capacity to absorb and concentrate glutamic acid can be used as an index of bacterial metabolism or of changes in bacterial cell walls affecting assimilation. The authors propose to use it to determine the effects of chemotherapeutic agents, differentiating between Gram-positive and Gram-negative bacteria, on the assimilatory processes of the former group. When 0·1 to 10 units per ml. of penicillin are added to growing cultures of *Staph. aureus* growth continues for 1 to 2 hours, though there is a steady loss of viability. If the organisms are grown in a casein digest containing 1% glucose and 0·1% " marmite " the concentration of glutamic acid in the organisms rises steadily throughout growth; on addition of penicillin the internal concentration of glutamic acid rises normally for the first hour or so, and then decreases rapidly, reaching a steady level as growth ceases. The organisms are then grown in a medium (nutrient-salt solution containing 1% glucose and 0·1% " marmite ") deficient in glutamic acid, with or without added penicillin. At intervals the organisms are centrifuged out, assayed for glutamic acid, and then incubated at 37° C. in a medium containing 0·5% glucose, suitable salts, and 200 μl. of glutamic acid per ml. After 1 hour the organisms are again centrifuged out and the internal glutamic acid redetermined. Cells to which no penicillin has been added take up 560 to 700 μl. of glutamic acid per 200 mg. in this test, and this capacity is unaffected by the addition of 200 units of penicillin per ml. Samples taken from cultures to which 10 units of penicillin per ml. have been added show that 30 minutes after the addition the capacity to assimilate glutamic acid has fallen to 14% of that of the penicillin-free controls; in 1 hour to 4%, in 1½ hours to 0%. Lower concentrations of penicillin take longer

to produce the effect. This loss of assimilatory power in cells pre-treated with penicillin (produced, presumably by changes in the cell wall preventing assimilation, either by combination of substances in the cell wall with penicillin, or reorganization of the cell-wall components under its influence) is unaffected by washing the cells in water or treating them with cysteine. Their content of glutamic acid is apparently metabolized normally whether they are affected by penicillin or not. The assimilation of lysine, which depends on a mechanism different from that by which glutamic acid is concentrated, is unaffected by pre-treatment of the cells with penicillin.

C. L. Oakley

STREPTOMYCIN

1748. **Streptomycin in the Treatment of Infections. A Report of One Thousand Cases**

The Committee on Chemotherapeutics and Other Agents, National Research Council. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 4–11 and 70–77, Sept. 7 and 14, 1946. 24 refs.

Streptomycin may be injected intramuscularly or subcutaneously, or into the subarachnoid space or the pleural or peritoneal cavities. The intramuscular route is the one of general choice. Following its injection streptomycin is excreted in the urine and bile. As it is necessary to maintain a concentration of the drug in the blood and tissues that is at least 4 to 8 times that required to inhibit organisms *in vitro*, injections must be repeated every 3 to 4 hours. The dosage depends on the type of infection and varies from 1 to 4 g. a day for 5 to 14 days. As resistance of infecting organisms to streptomycin occurs rapidly, maximum doses should be used at the beginning of treatment. In empyema or meningitis streptomycin should be injected directly into the pleural cavity or subarachnoid space. It is certainly the drug of choice in tularaemia, and has been most effective in meningitis due to *Haemophilus influenzae*. It should be used in all cases of bacteriaemia due to Gram-negative bacilli, especially when the primary lesion is in the genito-urinary tract, in which condition it is often effective when sulphonamides have failed. The main drawback to its use in urinary infections is the rapid development of resistant organisms. The results in the treatment of typhoid and Salmonella infections and in brucellosis are disappointing, and there is no conclusive evidence that the course of these infections is shortened by streptomycin. The results in experimental and clinical peritonitis and in pulmonary infections due to Friedländer's bacillus are sufficiently impressive to warrant a more extensive clinical study. Streptomycin has an inhibitory effect on the growth of the tubercle bacillus and should be helpful in tuberculosis when combined with other established methods of treatment, but a long-term programme of research is necessary before the true place of streptomycin in the treatment of this disease becomes clear. Histamine-like reactions, headache, nervous disturbances, fever, skin eruptions, and eosinophilia are common with streptomycin and are proportional to the dosage.

D. M. Dunlop

1749. **Streptomycin.** Civilian Production Administration, Washington, D.C. Chemical Division. Reference B. Aug. 1, 1946. 1 p.

The Civilian Production Administration in the U.S.A. has issued a brief directive of those conditions in which streptomycin is of proved value, those in which its value has not been definitely proved, and those where it is of doubtful value.

Group I: Indications.

1. All cases of tularaemia.
2. All cases of infection due to *Haemophilus influenzae*:
   Meningitis.
   Endocarditis.
   Laryngotracheitis.
   Urinary-tract infections.
   Pulmonary infections.
3. All cases of meningitis due to:
   Bacterium coli.
   Proteus.
   Friedländer's bacillus.
   Pseudomonas pyocyanea.
   Salmonella paratyphi B.
4. All cases of bacteriaemia due to Gram-negative organisms.
   Bacterium coli.
   Proteus.
   Bacterium aerogenes.
   Pseudomonas pyocyanea.
   Friedländer's bacillus.
5. Urinary-tract infections due to:
   Bacterium coli.
   Bacterium aerogenes.
   Proteus.
   Pseudomonas pyocyanea.
   Friedländer's bacillus.
   H. influenzae.

Group II: Conditions in which streptomycin has been found to be of help but in which its value is not definitely proved.

Peritonitis due to Gram-negative bacilli.
Pneumonia due to Friedländer's bacillus.
Liver abscess due to Gram-negative bacilli.
Cholangitis due to Gram-negative bacilli.
Infection of heart valves by penicillin-resistant but streptomycin-sensitive organisms.
Tuberculosis.
Chronic pulmonary infections due to mixed Gram-negative flora.
Empyema due to Gram-negative organisms.

Group III: Conditions in which streptomycin is of questionable value.

Typhoid.
Brucellosis.
Salmonella infections.

G. M. Findlay

1750. **Control of Salmonella Infections in Mice by Streptomycin**

C. A. Slanetz. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **62**, 248, June, 1946.

Streptomycin was incorporated in the drinking water of mice infected with *Salmonella enteritidis* for 7 days, so that the daily intake per mouse was 100 units. This treatment was found to sterilize the faecal cultures of 29 out of 30 mice.

G. A. H. Buttle

SULPHONAMIDES

1751. **" Sulpha-combination "—A New Chemotherapeutic Principle**
A. R. FRISK, G. HAGERMAN, S. HELANDER, and B. SJÖGREN. *British Medical Journal* [*Brit. med. J.*] **1**, 7–10, Jan. 4, 1947. 4 figs., 14 refs.

Renal complications and changes in the blood are liable to arise during sulphonamide therapy. An effort has been made to utilize a combination of sulphonamide drugs administered simultaneously and thereby obtain a high blood level without risk of kidney damage. The solubilities in urine of sulphadiazine, sulphamerazine, and sulphathiazole, together with those of their respective acetyl derivatives, were determined in relation to the *p*H. When mixtures of the compounds were used it appeared that all six drugs dissolved independently of one another. It would, therefore, be expected that mixtures of the compounds would be less likely to give rise to renal complications than would any one compound used alone, assuming that the sulphonamide level in the blood was the same in each case. This was investigated as follows:

It was found that in rabbits the intraperitoneal administration of 0·8 g. per kilo daily of sulphadiazine, or 0·6 g. of sulphamerazine, resulted in 100% of renal concretions in 9 and 10 days respectively. Similarly, 0·8 g. of sulphathiazole resulted in 67% of concretions in 16 days. The sulphonamide levels with these three drugs were 18, 8, and 6 mg. per 100 ml. of blood respectively. With " sulphadital ", a mixture of 37% sulphadiazine, 37% sulphathiazole, and 26% sulphamerazine, it was possible to administer 1 g. per kilo daily for 18 days without the formation of concretions, and the resulting blood level was 20 mg. per 100 ml.; while with 2 g. per kilo there were 40% of concretions and the resulting blood level was 41 mg. per 100 ml. The amount of sulphamerazine used in sulphadital is slightly less than the amounts of the two drugs, owing to the slower excretion of this compound, which results in a higher blood level. This mixture has given satisfactory results in several cases of pneumonia, and it has proved possible to obtain very much higher blood levels than with the drugs given separately. This method of administration of sulphonamide drugs appears greatly to lessen the risk of renal complication.

G. A. H. Buttle

1752. **Clinical Results Obtained by the Use of Sulfamethylpyrimidine (Percoccide).** [In English]
P. VAN DER MEER. *Acta Medica Scandinavica* [*Acta med. scand.*] **126**, 224–230, Nov. 9, 1946. 14 refs.

This is the report of a clinical trial in Holland of sulphamethylpyrimidine, commercially known as " percoccide ", a sulphonamide compound closely related to " sulphamezathine ", the abbreviated chemical name for which is sulphadimethylpyrimidine. The drug was used in 108 patients suffering from pneumonia, empyema, erysipelas, urinary infection, meningitis, and septicaemia. The dosage employed was that in common use for the better-known sulphonamides—6 to 8 g. orally in 24 hours till apyrexial, then 4 g. per day for a further 2 or 3 days. It may be administered intramuscularly, intravenously, or intrapleurally, in 5% solution. One case of pneumococcal septicaemia, after failing to respond to sulphapyridine, recovered with percoccide and received a total of 219 g. Another patient with septic endocarditis following tonsillitis received 299 g. [The organism in this case is not disclosed.] Toxic effects were rarely observed, but included gastro-intestinal upsets, rash, a granulocytosis, and haematuria. It would seem that percoccide, in activity and in degree of toxicity, compares favourably with other sulphonamides.

T. Semple

1753. **The Applicability of Skin Tests for Sulfonamide Hypersensitivity in Children**
H. W. FINK, I. BURTON, and W. E. WHEELER. *Journal of Immunology* [*J. Immunol.*] **54**, 65–67, Sept., 1946. 4 refs.

Few children show hypersensitivity reactions during treatment with sulphonamide drugs, but such reactions may be severe. The technique described by Leftwich was used in order to try to determine the presence of sensitivity. Nineteen children under the age of 12 were tested. They had had previous febrile reactions during the administration of either sulphathiazole (1 child) or sulphadiazine (18 children). Subsequently they were given the drug again, and 9 of them responded with immediate fever and a rash but 10 had no reactions. Serum was obtained aseptically and was used for testing within 5 hours. Normal serum was used as a control. The patients to be tested had been receiving a sulphonamide orally for at least 5 days. The " free " sulphonamide in the whole blood was more than 3 mg. per 100 ml. (usually 8 to 12 mg. per 100 ml.). Each patient was injected intradermally with 0·1 ml. of three sera on the same forearm: (1) normal serum, (2) sulphonamide-containing serum from an adult, and (3) sulphonamide-containing serum from a child. The original wheal and any erythema were measured; the sites were observed for 20 minutes and at intervals up to 24 hours. In no case was any difference detected between the reactions from the normal serum and from the sulphonamide-containing serum. There were no delayed or systemic reactions. It is concluded that Leftwich's method of skin testing for sulphonamide sensitivity is not applicable to children.

E. Lipman Cohen

1754. **Absorption and Excretion of Sulfathiadiazole and Sulfamethylthiadiazole after Oral Administration in Human Beings**
M. MEADS and M. FINLAND. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 900–909, Aug., 1946. 2 figs., 6 refs.

Sulphathiadiazole and sulphamethylthiadiazole administered to normal male subjects free from cardiac and renal insufficiency, at levels of 5 g. orally, were rapidly absorbed and excreted minimally conjugated in blood and urine. Only 4·5 to 8·1% of the sulphathiadiazole

administered to 2 subjects was recovered in the faeces, whereas often over 1% was detected in the urine within the first few hours, after ingestion of a single 5-g. dose of sulphamethylthiadiazole. At *p*H 5·5 the drug remained in solution in the urine, but 2 subjects voided large numbers of sulphamethylthiadiazole crystals, and 1 exhibited renal colic and haematuria following a single dose of 5 g.; but these complications were not seen during repeated administration of 1-g. doses at 4-hourly intervals. The high solubility throughout the urinary *p*H range and their proved effectiveness against coliform organisms suggest that sulphathiadiazole and its 5-methyl derivative deserve trials in the treatment of urinary tract infections, but that large individual doses should be avoided. *G. A. H. Buttle*

TOXICOLOGY

1755. **A Case of Thallium Poisoning.** (L'intoxication par le thallium)
J. L. DUCASSOU. *Journal de Médecine de Bordeaux et du Sud-Ouest* [*J. Méd. Bordeaux*] **123**, 336–340, Sept., 1946. 13 refs.

A case of thallium poisoning in a woman aged 26 is described. Gastro-intestinal symptoms appeared after 48 hours, peripheral neuritis of the lower extremities on the fourth and a severe stomatitis on the fifth day. The patient died on the ninth day of pulmonary congestion. The amount of ingested thallium, contained in about 40 g. of a vermin killer, is estimated at about 2·10 g.
A. Schott

1756. **Pathological Changes Induced by Lewisite and Allied Compounds**
G. R. CAMERON, H. M. CARLETON, and R. H. D. SHORT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 411–422, July, 1946. 8 figs., 2 refs.

This paper is concerned with a group of arsenical poisons which give constant and striking effects in laboratory animals when introduced through various routes. Lewisite I has been the most carefully studied, but sufficient evidence to establish similarity of toxicological action in the other members of the group (Lewisite II, phenyldichloroarsine, phenyldibromoarsine, phenyldifluoroarsine) is presented. All are fairly heavy liquids, with pungent odours, soluble in many organic solvents, and easily hydrolysed by water.

When applied to the skin, lewisite rapidly induces blistering with complete separation of the epidermis, subcutaneous oedema, and frequently haemorrhage. These effects are especially well developed in man, and when extensive may lead to much loss of plasma from the circulation and the consequences of this. Sloughing of skin, neuritis, and delayed arteritis are striking features in animal lesions. Hydrolysed lewisite (lewisite oxide) is absorbed rapidly and carried by the red corpuscles and plasma to the internal organs, excretion occurring chiefly by way of the liver and kidneys. Apparently detoxication is feebly developed in the liver, for most of the lewisite oxide is excreted unchanged in the bile, thereby damaging the liver cells and the lining of the bile passage and gall-bladder. Acute hepatic necrosis and haemorrhagic cholecystitis and choledochitis are therefore characteristic features of lewisite poisoning. In passing through the kidneys most of the lewisite oxide is converted into a less noxious compound characterized by a quinquivalent arsenic atom.

Other signs of lewisite intoxication include a tendency to haemolysis causing a mild degree of haemolytic anaemia and occasionally an acute haemolytic crisis, extensive damage of capillaries with widespread haemorrhage, loss of plasma into serous cavities, and pulmonary oedema resulting when severe in a shock-like condition which the authors call " lewisite shock ". Ingestion of lewisite or hydrolysed lewisite in small amounts leads to acute haemorrhagic gastritis with necrosis of the lining epithelium and submucous oedema. Perforation is likely to follow with larger doses. Pyloric spasm is pronounced and prevents the passage of the irritant into the duodenum, so that intestinal lesions are slight or absent. Lewisite, however, is highly destructive if it reaches the intestines. Systemic effects follow absorption from the alimentary canal.

Inhalation of lewisite vapour or droplets induces severe laryngeal spasm and may cause death from asphyxia. Nasal absorption is followed by acute mucopurulent rhinitis, the accessory sinuses also being affected. If the lower air passages are penetrated there follows rapidly acute pharyngitis, laryngitis, and tracheitis with false-membrane formation and often serious ulceration and oedema of the wall of these structures. Acute fibrinous bronchitis is pronounced, and a cast may spread to the terminal bronchi, leading to pulmonary collapse. Pulmonary oedema is common during the first 24 hours after inhalation, but it soon passes into acute bronchopneumonia. Pleural effusion is not uncommon, and sometimes empyema is a complication. These lesions closely resemble those following inhalation of mustard gas. Systemic effects are rare.

[This paper includes a useful table of minimal lethal doses for a variety of animals. No information exists about the fatal dose for man, though quite likely it is a few milligrammes per kilo of body weight orally.]
G. R. Cameron

1757. **A Case of Acute Emetine Poisoning**
A. L. WAHI. *Indian Medical Journal* [*Indian med. J.*] **41**, 13, Jan. 15, 1947.

A Hindu woman about 60 years old was given two intramuscular injections of 1 gr. (65 mg.) of emetine hydrochloride on 2 successive days. She reacted with a slight rise in temperature, a pulse rate of 120, urticaria involving the palms of the hand and soles of the feet, and acute glossitis. *G. M. Findlay*

1758. **Biochemical Research at Oxford upon Mustard Gas**
R. A. PETERS. *Nature* [*Nature, Lond.*] **159**, 149–151, Feb. 1, 1947. 26 refs.

1759. **Some Cases of Ethylene Glycol Poisoning.** (Några fall av etylenglykolförgiftning)
C. WIDMAN. *Nordisk Medicin* [*Nord. Med.*] **31**, 1921–1924, Aug. 23, 1946. 1 fig., 30 refs.

Three patients, aged 33, 42, and 46, drank ethylene glycol; in 1 case the volume was estimated at 100 ml. No symptoms developed for about 12 hours; then incoherence, incoordination, and hallucinations appeared, followed by vomiting of blood, confusion, coma, and death, which occurred between 30 and 144 hours after ingestion. Necropsy in 2 cases showed, as the principal lesion, extensive necrosis of the epithelium of the renal tubules with deposition of crystals of calcium oxalate in their lumina. *G. Discombe*

1760. **Influence of Experimental Peroral Alcohol Intoxication on Storage and Absorption of Vitamin A.** (Om den experimentelle, perorale Alkoholintoxikations Indflydelse paa Aflejring og Resorption af A-Vitamin)
H. B. JENSEN and O. WANSCHER. *Nordisk Medicin* [*Nord. Med.*] **31**, 1811–1816, Aug. 16, 1946. 5 figs., 17 refs.

The effect of continual administration of alcohol to rabbits was investigated to decide whether damage to the gastric mucosa could restrict the absorption of vitamin A, with the possible development of portal cirrhosis or a condition resembling pellagra. Nine-week-old rabbits were placed on a diet free from vitamin A and with a known daily supplement of vitamin added; 72% alcohol was then given daily in amounts increasing from 5 to 10 ml. A control group received no alcohol; 10 animals survived the experiment. At the end of the experiment the animals were killed and the vitamin-A content of their livers was determined. It was found to be lower in the alcohol-treated animals (14 to 46 units per g.) than in the controls (80 to 250 units per g.). The alcohol-treated animals also failed to gain weight in spite of adequate calorie intake.

In a further experiment the administration of alcohol for a short period (2 to 10 days) failed significantly to reduce the existing vitamin-A content of the rabbits' liver. The effect of prolonged administration of alcohol upon the absorption of vitamin A from the stomach was investigated by giving 2 rabbits 10 ml. of alcohol daily for 14 weeks. Vitamin A was then given (35,000 units in 2 days), and the vitamin-A content of the liver was determined as before. No significant difference was found between the test animals and 2 controls. In similar experiments young rats were put on a diet deficient in vitamin A until avitaminosis developed. Vitamin A was then given (1,500 units per day); after 4 weeks alcohol was given for 4 to 12 weeks in doses increasing from 0·8 to 2·5 ml. per day, the administration of vitamin A continuing meanwhile. At the conclusion of the experiment the 17 test animals showed no significant reduction in the vitamin-A content of the liver compared with the 23 controls.

It appears from the above work that the administration of alcohol does not deplete the existing stocks of vitamin A in the liver or hinder its absorption from the stomach. A reduction in the vitamin content of the liver is seen only when alcohol and the vitamin are given simultaneously, suggesting that it is the actual deposition of vitamin in the liver which is affected. One-half of the alcohol-treated animals showed lesions in the skin and central nervous system; the liver exhibited occasional round-cell infiltration, but in no case was there cirrhosis.
D. J. Bauer

1761. **The Physiologic Properties of Thioglycolic Acid and Thioglycolates**
C. P. MCCORD. *Industrial Medicine* [*Industr. Med.*] **15**, 669–676, Dec., 1946.

Thioglycolic acid, discovered in 1862, has recently been used in the form of thioglycolates by hairdressers for permanent waving, curling, and artificial straightening of hair. This is a cold wave process, requiring no apparatus beyond rollers, and can therefore be done in the home. Its simplicity suggests that the method will replace hot waving with curling-tongs. In beauty shops the professional operator may do the hair of 6 to 8 women in a day; contact with thioglycolates is thus established, and a new occupational hazard created. The risk to the user is obviously less. Effects on the hair, of value to the hairdresser, are to decrease tensile strength and increase elasticity for at least 30 days. There is no apparent evidence of permanent hair damage. Thioglycolic acid in relatively low concentration is toxic. Patch tests showed that ammonium thioglycolate ($HSCH_2CO_2NH_4$) was apparently more irritating to the skin than the sodium salt; allergenic properties of both acid and salts were slight or non-existent. The total quantity of hydrogen sulphide arising after induced decomposition of either thioglycolic acid or thioglycolates is insufficient to produce systemic poisoning.
Donald Stewart

1762. **Does Welder's Disease Really Exist?** (Existe-t-il une maladie des soudeurs?)
A. FEIL. *Presse Médicale* [*Presse méd.*] **54**, 598, Sept. 14, 1946.

The author doubts the existence of a specific " welder's disease " apart from that which occurs as a result of handling toxic substances, such as lead. Arc welders' methods of working, their booths, screens, and goggles, are described. The fumes from the electrode metal and its covering did not contain toxic substances. An inquiry was started on 67 arc welders, most of whom had been working for at least 5 years, and some for 15 or 20 years. Certain particular disorders have commonly been attributed to arc welding—namely, ocular lesions, dyspepsias, pneumoconiosis, metal-fume fever, and impotence; no serious intoxications or pathological manifestations were found. Frequently welders suffer from the condition of " flash-eye " (*coup d'arc*) from exposure to ultraviolet and infra-red radiations, with characteristic symptoms and a delayed and transient kerato-conjunctivitis. Weakness of vision, especially at night, was found in 20%. Digestive disturbances occurred in 37%. Cough is fairly common (37%), and

in radiographs of 1 in 10 or 12 workers there is an appearance of nodulation (*granitée*), which is due to iron oxide, since the dust contains 51% of iron oxide and only 1·5% of silicon dioxide. These small nodules at necropsy do not show the typical connective-tissue proliferation of silicosis. There was little evidence of abnormalities in the blood or in the nervous system. The evidence that welding causes sexual dysfunction was slender, for only 4 to 5% complained of impotence, and this could be attributed to other causes. Intoxication from lead, phosphorus, and arsenic is possible, but only because of contact with these substances and not specifically because of welding. The ocular manifestations alone seem to be directly caused by the occupation. The risks of welding have been over-emphasized. *J. N. Agate*

1763. **Effect of Citrate on the Reactions of Lead with Blood Cells and Plasma**
R. A. MORTENSEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 315–320, Sept., 1946. 1 fig., 13 refs.

In view of recent reports that the administration of citrate reduces the concentration of lead in the blood and increases its excretion, the effect of citrate upon lead metabolism was considered to merit further investigation. All the experiments were made *in vitro* with freshly drawn human blood at 37·5° C., heparin being used as the anticoagulant. Solutions of lead chloride and sodium citrate were added in small amounts with micropipettes. Lead analyses were made by using radium D, an isotope of lead, as an indicator, the activity of which was measured with a Geiger-Müller counter. The results were as follows. When the added lead was of such a concentration that a large fraction remained in the plasma, the addition of citrate increased the percentage of lead taken up by the cells. The addition of citrate greatly increased the ability of the cells to combine with lead previously mixed with plasma or Ringer's solution. Lead was readily transferred from cells to plasma, but citrate had little or no effect on this process. The proportion of non-diffusible lead in plasma and serum, as determined by ultrafiltration, was reduced by citrate.

It is suggested that citrate may promote the mobilization of lead by increasing the capacity of the cells to take it up from the tissue fluid, and that this factor, together with the increased proportion of diffusible lead produced by citrate, may result in a free exchange of lead between the tissues and the blood. The increased diffusibility, moreover, should facilitate excretion. While the range of citrate concentrations included some values considerably above those attained in the body, it is known that the administration of sodium citrate results in an elevation of the blood citrate and should therefore influence the behaviour of lead in the blood to a corresponding extent. It is thought that the citrate ion acts by serving as a carrier which takes up and then releases lead ion to the cells. *L. J. Davis*

1764. **The Estimation of Traces of Mercury in Urine**
R. F. MILTON and J. L. HOSKINS. *Analyst* [*Analyst*] **72**, 6–10, Jan., 1947. 3 refs.

THERAPEUTICS

1765. **Carbolized Antirabies Vaccine Prepared from Other Nervous Substances than those of the Rabbit. Elimination of Shock in the Course of Treatment.** (Vaccin antirabique phéniqué à base de substances nerveuses autres que celles du lapin. Disparition des incidents de choc)
J. H. RAYNAL and Y. C. LIEOU. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **72**, 832–835, Sept.–Oct., 1946. 1 ref.

The authors claim that the occurrence of shock after injection of phenolized rabies vaccine can be entirely avoided by the use of sheep or dog brain instead of rabbit brain in preparing the vaccine. Dilution of rabbit-brain vaccine immediately before use slightly reduces the incidence of shock. *C. L. Oakley*

1766. **The Application of Tissue Culture to Problems of Immunity. II. Experimental Study of the Action of an Antileucocytic Serum.** (Cultures de tissus appliquées à la solution de problèmes immunologiques. II. Étude d'un sérum antileucocytaire; mécanisme de son action *in vitro*. Contribution à l'étude des phénomènes anaphylactiques en cultures de tissus)
E. LASFARGUES and A. DELAUNAY. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **72**, 828–832, Sept.–Oct., 1946. 2 refs.

Hanging-drop tissue cultures of guinea-pig spleen fragments in a mixture of two drops of guinea-pig plasma, two drops of spleen juice, and one drop of rabbit antileucocytic serum show reduced migration of polymorphonuclear leucocytes and monocytes as compared with controls in which Ringer's solution replaces the antileucocytic serum; the migrating cells are damaged, rounded off, and granular. Re-transplantation of explants in antileucocytic serum to the control medium leads to slow poor growth. This effect of antileucocytic serum on leucocytes is not increased by complement, which, possibly by diluting the antileucocytic serum, increases the rate and quantity of cellular migration.

Noting that antileucocytic sera contain both Forssman antibodies and specific antileucocytic substances, the authors attempt to determine whether the action of antileucocytic serum is purely lytic or is due to antigen–antibody combination in the leucocyte; that is, something resembling anaphylaxis. Forssman antibody, though able to combine with the Forssman antigen in leucocytes, has no damaging effect on them, while antileucocytic sera from which the Forssman antibody has been removed by absorption with sheep's red cells still damages leucocytes. To reverse the experiment, guinea-pigs were immunized with horse serum until injection of 0·5 ml. produced an Arthus phenomenon. Splenic cultures from these guinea-pigs grown in a medium containing horse serum showed no necrosis and grew rather better than explants in the control medium. The Arthus phenomenon cannot therefore be produced *in vitro*. *C. L. Oakley*

1767. **Sera Stabilized by Formol and Heat: Practical Application of the Method to Bovine and Human Sera.** (Contribution à l'étude des sérums stabilisés par l'action combinée du formol et de la chaleur: Applications pratiques au sérum de bovidés et au sérum humain)
CH. MÉRIEUX. *Bulletin de l'Académie de Médecine* [*Bull. Acad. Méd. Paris*] **130**, 506–507, 1946. 9 refs.

During the recent war bovine serum was treated with the addition of 0·05% formol and heated to 56° C. (time of heating not stated). Serum treated in this way could be injected intravenously into rabbits in quantities of 100 ml. and over without noticeable after-effects. Such serum has been used on a large scale to treat malnutrition in children, but whether by mouth or parenterally is not stated. Human serum obtained by 30 minutes' centrifuging at 2,000 revolutions per minute of fresh blood was passed through Seitz filters, heated to 56° C., and sealed in 500-ml. bottles after addition of 0·05% formol. This serum was subsequently used for urgent transfusions in members of the Resistance Movement, but conditions did not permit detailed assay of results. Clinical observations showed that the preparation was efficient and harmless. A few bottles have been recovered by the author 2 years after preparation and the contents were found to be well preserved. The author considers this serum an ideal transfusion medium and considers that its use will diminish considerably the risk of transfusion jaundice. *G. Schoenewald*

1768. **Blood Transfusion Studies. I. The Differentiation of Hemolytic and Nonhemolytic Transfusion Reactions**
E. B. FLINK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 1067–1073, Oct., 1946. 21 refs.

Most transfusion reactions fall into the following groups: (1) simple febrile reactions due to pyrogenic substances in the solutions; (2) allergic reactions, both anaphylactic and urticarial; (3) circulatory reactions from too rapid administration, particularly to seriously anaemic and debilitated patients; and (4) febrile reactions accompanied by intravascular haemolysis. Separation of haemolytic reactions from simple febrile reactions is often impossible from clinical signs and symptoms alone. In this investigation 58 blood transfusions were given to anaemic patients, blood specimens being obtained immediately before transfusion and within an hour of the end. The haemoglobin concentration in the plasma was determined colorimetrically by means of a photoelectric colorimeter. Despite care in the taking of samples, 10 out of 58 showed 3 to 12 mg. of haemoglobin per 100 ml. in the pre-transfusion plasma sample; the remaining 48 cases showed less than 3 mg. per 100 ml. It was noted that haemoglobin could not be detected by the naked eye unless the level exceeded 20 to 25 mg. per 100 ml. of plasma. In samples taken within 1 hour of the end of transfusion much the same range of values was found, the average being only 1 mg. per 100 ml. higher than the average pre-transfusion figure. In an additional 19 patients who developed febrile reactions after transfusion a similar range of values for plasma haemoglobin was found, demonstrating the non-haemolytic nature of the reactions. In 5 haemolytic reactions the plasma haemoglobin level varied between 36 and 254 mg. per 100 ml., but often samples were only taken some hours after the transfusion, and it is well known that haemoglobin is rapidly cleared from the plasma. It will be noted that in all these cases the degree of haemoglobinaemia was sufficient to be detectable by the naked eye.

[This work confirms the well-established value of examining a carefully taken sample of plasma for naked-eye haemolysis as a means of determining whether a given adverse reaction to transfusion is or is not haemolytic.] *P. L. Mollison*

1769. **Blood Transfusion Studies. II. The Survival of Fresh and Stored Transfused Erythrocytes as Determined by Urobilinogen Excretion**
E. B. FLINK and K. B. SKUBI. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 1074–1078, Oct., 1946. 17 refs.

Following the transfusion of blood stored for 6 to 8 days in sodium citrate alone there is a regular increase in serum bilirubin concentration, reaching a maximum approximately 5 hours after transfusion, and a less regular increase in the excretion of urobilinogen in the faeces.

[It is difficult to see why blood stored in sodium citrate alone was used in these experiments. There is ample evidence, particularly from cell-survival experiments, that sodium citrate is a very poor preservative compared with solutions to which glucose, or better still glucose with acid, have been added, and blood that is to be stored should never be taken into plain trisodium citrate.] *P. L. Mollison*

1770. **Medical Aspects of Mustard Gas Poisoning**
H. CULLUMBINE. *Nature* [*Nature, Lond.*] **159**, 151–153, Feb. 1, 1947.

1771. **The Determination of Mercury in Air**
E. C. BARNES. *Journal of Industrial Hygiene and Toxicology* [*J. Industr. Hyg.*] **28**, 257–261, Nov., 1946. 10 refs.

1772. **Industrial Exposure to Lead**
M. R. MAYERS. *Occupational Medicine* [*Occup. med.*] **3**, 77–83, Jan., 1947.

1773. **Biological Effect of Some DDT Derivatives.** (Zur biologischen Wirkung einiger DDT-Derivate.)
R. DOMENJOZ. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **73**, 128–146, Dec. 1, 1946. 12 refs.

1773a. **The Pharmacologic Action of Certain Analogues and Derivatives of DDT**
M. I. SMITH, H. BAUER, E. F. STOHLMAN, and R. D. LILLIE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **88**, 359–365, Dec., 1946. 10 refs.

Medical Jurisprudence

1774. **Medical Experiments on Human Beings in Concentration Camps in Nazi Germany**
K. MELLANBY. *British Medical Journal* [*Brit. med. J.*] **1**, 148–150, Jan. 25, 1947. 3 figs., 1 ref.

The judgment of the International Military Tribunal which tried Goering and his colleagues contained many references to medical experiments on human beings (the fact of which was found proved), and to the responsibility for them of the various Nazi leaders and organizations. There is no doubt that thousands died as involuntary victims of experiments and that many prisoners were put to death by methods devized and executed by physicians engaged in " research " into the problem of killing as expeditiously as possible.

Independently of the International Military Tribunal each occupying Power set up its own tribunals to try the " lesser fry " ; these tribunals have completed many cases, convicting in some and acquitting in others. Of persons already convicted the most noteworthy was Dr. Klaus Schilling, the eminent malariologist, who was executed early in 1946 for his part in experiments with malaria in Dachau. With a greater claim to the title of scientist than most of the experimenters, he used a mild strain of benign tertian malaria, and seems to have administered drugs carefully and scientifically. Accused at a trial held by the United States authorities of having caused many deaths, it was considered that " although Dr. Schilling's motive may have been sincere and purely a scientific one, his activities exemplified the Nazi schema which existed at Dachau. The part he played in that schema is clear ". These tribunals, the legal basis of which is difficult to explain briefly, do not conform to the code of any country but follow laws set forth by the Allied Control Council in 1945 and attempt to abide by resolutions of international conventions such as that of The Hague (1907). While some jurists feel that the situation is unsatisfactory and may lead to abuses, the author's impression is that the tribunals make every effort to give the defendants a just hearing.

In one of the trials there were 23 defendants, and a list is given of the various medical experiments carried out. These include experiments on toleration of high altitudes, resistance to freezing, malaria infection, mustard gas, chemotherapy and regeneration of tissues in artificially inflicted wounds, the potability of sea water, infective hepatitis, methods of sterilization, epidemic typhus, effects of poison, the treatment of burns caused by incendiary bombs, and the various " euthanasia " programmes carried out on Poles and " useless eaters ". The author quotes from the prosecution in the current trial, stating that the primary objects of the prosecution are to give clear and public proof of these experiments and to demonstrate that the whole body of organized medicine in Nazi Germany was behind the policy. A description (with diagram) is given of the State organization responsible for the experiments. Hitler knew and approved of them but the more immediate responsibility lay with Himmler, who took a considerable though uninformed interest in research. His constant demand for results did much to ensure that the experiments were of the minimum scientific value. The defendant Karl Brandt occupied the highest position in German medicine. As *Reichskommissar* for Health and Sanitation he had complete control over every medical activity. The defendant Rostock worked under him and was in charge of medical research. The two main branches of the medical services were those of the armed Forces and the civilian services; their heads were responsible to Keitel and the Minister of the Interior respectively on the one hand, and both, on the other, to Brandt.

The prosecution has used the word " thanatology " (the science of producing death) to describe the experiments, alleging that in the majority of cases the object was to produce speedy extermination, which seems true of some investigations. As to the allegation that practically no results of value were obtained, this requires further study as, while a useful evaluation of various typhus vaccines was arrived at, other work is unlikely to be of use. Most of the work was badly planned and carried out under constant political pressure. Also, the victims were prisoners and not volunteers such as are used in other countries; they looked on sabotage, if possible, as a duty. *P. N. Meenan*

1775. **Intracranial Haemorrhages after Death by Burning**
B. F. SAMPSON. *Clinical Proceedings* [*Clin. Proc.*] **5**, 189–194, July, 1946. 4 figs.

Extradural haemorrhages in association with heat fractures of the skull in 3 women burned to death in a shed at their home are described briefly by the author, who himself performed the necropsies. He rightly draws attention to the fact that fissure fractures of the skull occur commonly after exposure to fierce heat, and emphasizes their distinction from the depressed or comminuted fractures of blunt injury.

[Unfortunately, by failing to draw attention to the existence of any literature—small as it may be—on the subject of burns and associated haemorrhages between the skull and the dura, the author has given this article the air of an original observation, which it is not. The subject receives passing reference in two of the shorter standard British textbooks of forensic medicine, and also has a small literature. Sampson draws the correct conclusions, but does not offer the common explanation—that these haemorrhages are due to boiling of the blood, its escape through heat fractures or tears in the dural vessels, and its fixation by heat after raising the dura from the skull under pressure. Only good can come of an article drawing further attention to the existence of this heat phenomenon and to its forensic significance.]
Keith Simpson

Radiology

1776. **Therapeutic Possibilities of Radio-Phosphorus**
J. S. MITCHELL. *British Medical Journal* [*Brit. med. J.*] **1**, 250–251, Feb. 15, 1947. 8 refs.

Recent literature, principally American, on radio-phosphorus is reviewed. Ordinary phosphorus exposed to slow neutrons in a " pile " can be activated to about one-third of a curie of P^{32} per g. of phosphorus. The radio-phosphorus is used in the form of an isotonic disodium hydrogen phosphate solution (15 mg. per ml.) with initial activity of about 300 microcuries per ml. P^{32} has a half-life of 14·3 days and emits beta rays of maximum energy 1·7 mev. and mean energy about 0·7 mev. One microcurie of P^{32} per g. of tissue delivers 43 r per day; 1·13 microcuries destroyed per kilo of tissue deliver 1 r; if 1 millicurie is retained for 24 hours by a patient weighing 70 kg., approximately 0·6 roentgen equivalents of irradiation are delivered to the whole body.

Clinically the radioactive phosphate solution is best given intravenously using a fractionated treatment with unit doses of 0·5 to 2 millicuries. For chronic myeloid leukaemia 11·8 millicuries has been administered in 78 days. For polycythaemia vera a single dose of 3·5 to 4 millicuries may suffice. Early optimism regarding the therapeutic value of radio-phosphorus is not yet justified; only in the treatment of polycythaemia vera is it now regarded as the best therapeutic agent at present available. It is hardly to be expected that radio-elements administered as inorganic compounds will be sufficiently selectively absorbed by cancer tissue, and further progress is likely to lie in the search for organic compounds which are selectively picked up by cancer tissue.

D. E. Lea

1777. **The Effect of Gamma Radiation on Mitosis *in Vitro***
I. SIMON-REUSS and F. G. SPEAR. *British Journal of Radiology* [*Brit. J. Radiol.*] **20**, 63–70, Feb., 1947. 12 figs., 16 refs.

Canti and Spear plotted the graph of results of irradiation on mitosis. Read suggested that the peculiarities of this graph are due to the presence of a few abnormal mitotic figures among unaffected cells, because such abnormality interferes with the time taken for such a cell to complete division. Choroid and sclerotic tissue of 10- to 11-day-old chick embryos was cultured, and a photographic study made of the effects of doses ranging from 55 to 1,320 r of gamma radiation, delivered at 22 r per minute, to determine the average duration of mitosis before and after exposure. This was compared with similarly irradiated cultures fixed and stained for histological examination at various intervals after exposure; these were investigated quantitatively and qualitatively. For quantitative observation the total number of mitotic cells in the irradiated specimen was compared with control specimens from a similar group of unirradiated cells.

A large number of abnormal mitotic figures were seen at intervals after irradiation, when a corresponding timing experiment showed that the majority of observed dividing cells completed division within normal time limits. Expressed in a graph, these observations indicate that after each exposure there is a drop in the number of normal mitotic cells, and that even the lowest dose of irradiation causes an appreciable number of mitotic abnormalities. Types of abnormality noted were: clumped metaphases, giant metaphases, unseparated telophases, binucleate daughter cells, fragmentation of chromosomes, and breaking up of cells. Gross individual abnormality is associated with high radiation dosage, but these experiments show that even with low dosage a proportion of cells is affected either structurally or functionally. Some of these cells, which on staining reveal recognizable abnormalities, are still able to complete division within normal time limits. The duration of normal mitosis *in vitro* agreed with the findings of other observers. Under comparable culture and temperature conditions the average is 18 to 20 minutes for the total process, with 16 and 40 minutes as outside limits.

D. G. Williams

1778. **Artificial Sunlight Treatment. The Proper Perspective**
L. SCHMIDT. *British Journal of Physical Medicine and Industrial Hygiene* [*Brit. J. phys. Med.*] **9**, 175–179, Nov.–Dec., 1946. 2 figs., 9 refs.

The healing effect of sunlight has been known and described since the days of ancient Greece, but Niels Finsen of Copenhagen first employed artificial light irradiation as a therapeutic agent. Its application to improve health and to prevent sickness has gradually increased during the past 20 years, but the effectiveness of such treatment has been recently questioned (Colebrook, *Rep. industr. Hlth Res. Bd.*, 1946, **89**). The author briefly considers the spectrum and the action of electromagnetic waves of different wave lengths. The local and general effects of ultraviolet irradiation are recorded. Natural sunlight, mercury-vapour arc lamps, and carbon arc lamps are the common sources of radiant energy, and differences in their output are dealt with. In discussing the qualitative and quantitative aspects of dosage it is felt that the erythemal effect is the limiting factor in the useful application of actinic rays for prophylactic purposes. The optimal effect of irradiation cannot be achieved if the minimum perceptible erythema dosage is reached or exceeded. The author's practice is to arrange for daily irradiation with short duration of exposure. The composition of the rays of the mercury-vapour lamps is quite different from that of normal sunlight, and, in order to reproduce the solar spectrum, the

author uses low-pressure mercury-vapour lamps combined with carbon arc lamps, having carbons impregnated with elements of the cerium group. Colebrook's work is criticized on the ground of its statistical approach, the failure to consider subjective effects and biochemical findings, and the technical basis of the inquiry.

A. Thelwall Jones

1779. **Secondary Emanatory Phenomena in the Blood of Irradiated Subjects**

M. A. COOKE. *British Journal of Physical Medicine and Industrial Hygiene* [*Brit. J. phys. Med.*] **9**, 172–174, Nov.–Dec., 1946. 9 figs., 5 refs.

Previous workers have been able to fog a photographic film by exposing it to blood previously irradiated with ultraviolet light. In the present work such phosphorescent phenomena have been sought in the blood of irradiated patients. Photographic films were exposed to specimens of blood taken from patients before and after ultraviolet irradiation and from a control. Fogging of the films indicates there is some emanation from the blood of such patients after irradiation. This emanation is quite marked after 1 week of general irradiation, and persists in the blood for several days, even after a short course of therapy. The possible significance of this phenomenon in the interpretation of the beneficial effect of general irradiation on local conditions and in the aetiology of lupus erythematosus is discussed.

[Experimental details in this paper are scanty, and there is no indication of the photographic technique used. No attempt is made to investigate the nature of the "emanations". A phosphorescence over such a long period as that indicated must be regarded as a very unusual phenomenon.] *J. E. Roberts*

1780. **Retrograde Abdominal Aortography. A Contribution to the Study of the Abdominal Aorta and Iliac Arteries**

P. L. FARIÑAS. *Radiology* [*Radiology*] **47**, 344–348, Oct., 1946. 8 figs.

Retrograde abdominal aortography is a method used for the study of pathological changes in the aorta and iliac arteries. The femoral artery is exposed by blunt dissection under local analgesia at the level of Scarpa's triangle, and a trocar 1·5 mm. in diameter is introduced, through which is injected 50 ml. of a 70% solution of "diodrast" in 2½ to 3 seconds. A tourniquet is applied to each limb below the site of injection in order to prevent the passage of the contrast medium into the arteries. The Trendelenburg position may be required in certain cases. To avoid changes in pressure during the injection the author has designed an apparatus that maintains a steady rate of flow. The first film is taken when 40 ml. of the opaque substance has been injected, and a second one immediately afterwards, a fast film-changer being necessary. Premedication consists in the administration of phenobarbitone the previous night and morphine hypodermically an hour before the injection.

The changes consequent upon syphilitic arteritis, in the form of dilatation or obliteration, can be demonstrated by this method; the presence and extent of a thrombus can be ascertained, and in such cases the increased collateral circulation becomes apparent. The author has observed valvular kinks that considerably retard circulation and claims that their surgical removal has been shown to benefit greatly the circulation of both limbs. *L. G. Blair*

1781. **Redundant Duodenum. A Radiographic Study**

I. H. SLATER and A. LAUTKIN. *United States Naval Medical Bulletin* [*Nav. med. Bull., Wash.*] **46**, 1651–1657, Nov., 1946. 3 figs., 12 refs.

In 1,000 consecutive barium meal examinations in a U.S. naval hospital the presence of an elongated first part of the duodenum forming an extra V- or U-shaped loop was reported 20 times. This figure of 2% corresponds with other estimates in the literature. The authors call attention to the anomaly, which, in several cases, led to a mistaken diagnosis of duodenal ulcer either because the duodenal cap was kinked or because the fold pattern of the redundant loop showed through the fold pattern of the cap. Four case histories are given. No typical symptoms were associated with these cases, and it is considered unlikely that the malformation caused symptoms, since in 6 out of the 22 cases, there was some other definite lesion, this being in the same proportion as for the total series of 1,000 cases, 248 of which showed a definite lesion. The anatomy and embryology of the first part of the duodenum is described.

[The views of the authors coincide with orthodox British radiological teaching.] *Denys Jennings*

1782. **The Roentgenographic Appearance of the Falx Cerebri**

E. G. ROBERTSON. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **56**, 320–323, Sept., 1946. 4 figs.

The normal falx cerebri is usually visible in antero-posterior or postero-anterior radiographs as a narrow thread-like shadow in the midline, extending to within 1 cm. of the vertex and disappearing below at a variable distance above the crista galli or merging into the shadow of its bony attachment. It may be seen in young children and is not dependent on the presence of pathological calcification; the shadow depends on the relative opacities of the fibrous tissue of the falx and the brain substance as can be shown in a film taken with a falx stretched horizontally behind a normal skull.

The shadow was seen in one or more films in 65 out of 100 patients in whom two or three radiographs had been taken, and short segments of it were also seen in 28 cases. In 9 cases the falx was not seen, usually because of slight rotation so that the rays were not tangential to the line of the falx. The falx was visible in a smaller percentage of patients with cerebral tumours—28 of 50 cases—and in 13 of these lateral displacement was seen. Displacement of the shadow probably accounted for the greater difficulty of visualization. *J. W. Litchfield*

Pathology

1783. **The Influence of Liver *L. casei* Factor on Spontaneous Breast Cancer in Mice**
R. LEWISOHN, C. LEUCHTENBERGER, R. LEUCHTENBERGER, and J. C. KERESZTESY. *Science* [*Science*] **104**, 436–437, Nov. 8, 1946. 3 refs.

The authors have previously shown that intravenous injections of crystalline, or " fermentation ", *Lactobacillus casei* factor led to complete regression of spontaneous breast cancer in mice in about one-third of the animals. The effect of " liver " *L. casei* factor in this respect is now reported. Ninety-eight mice bearing single spontaneous breast cancers, confirmed by biopsy, were divided into 3 groups of approximately equal numbers which were given daily intravenous injections of 5 μg. of liver *L. casei* factor, 100 μg. liver *L. casei* factor, and 5μg. of crystalline fermentation *L. casei* factor, respectively. The periods of treatment extended from 4 to 6 weeks. A control group of 71 mice of the same strain was observed during the period of the experiment.

It was found that while the fermentation *L. casei* factor resulted in complete regression of the tumours in 11 of 28 mice, such an effect occurred in only 1 of the 70 mice receiving liver *L. casei* factor. The group receiving liver *L. casei* factor in 100-μg. doses had a significantly shorter mean life span than any of the other groups, and the primary tumours in this group grew more rapidly than the tumours of untreated controls. It is pointed out that no conclusions should be drawn from these experiments as to the action of the liver *L. casei* factor on human cancer.

[Although synthetic folic acid is said to be identical with the liver *L. casei* factor, it is not clear in the text whether the synthetic preparation was used in these experiments.] *L. J. Davis*

1784. **Necropsies on Okinawans. Anatomic and Pathologic Observations**
P. E. STEINER. *Archives of Pathology* [*Arch. Path., Chicago*] **42**, 359–380, Oct., 1946.

During the period June 13 to July 30, 1945, the author performed necropsies on 150 Okinawans—51 males and 99 females. Very complete examinations were carried out, and the author has carefully analysed his findings and compared them with information obtained from physicians on the island. The two points of view were in agreement in many cases.

Among the causes of death there were 100 injuries and 36 medical conditions; in 14 instances both were present. Anatomically the bodies showed evidence of adaptation to the strenuous life of the natives. Congenital anomalies were fairly numerous and resembled those encountered elsewhere except for a curious S-shaped bend in the hepatic flexure of the colon which was frequently seen. Infections—the largest group—included tuberculosis, pneumonia, dysentery, and tetanus. Certain infections, such as yaws, malaria, tsutsugamushi fever, Japanese encephalitis B, and trematode infestation, were not found. Of neoplasms, only one case of uterine fibroids was met with, although physicians on the island asserted that carcinoma was fairly common among old people and involved the stomach, uterus, breast, oesophagus, and tongue mainly. Leukaemia had never been seen. Degenerative conditions, like arteriosclerosis, hypertension, and cardio-renal disease, were rare and appeared very late in life. Six cases of cirrhosis of the liver were seen; lithiasis was uncommon in either the biliary or the renal tracts. Endocrine disorders were very uncommon, and so were conditions like cervical erosion, cystic ovaries, uterine fibroids, and mammary hyperplasia—all common enough in more civilized communities. On the other hand, 64·7% of the cases showed intestinal helminth infestation, mainly due to *Ascaris lumbricoides*; filariasis, though fairly common, led to very little elephantiasis. *R. B. T. Baldwin*

1785. **On the Production of Sarcoma with Wheat Germ Oil**
P. N. HARRIS. *Cancer Research* [*Cancer Res.*] **7**, 26–34, Jan., 1947. 16 figs., 23 refs.

Of 370 mice which received intraperitoneal or subcutaneous injections of wheat-germ oil 2 developed tumours after 8 and 12 months. Of 360 rats similarly treated 16 developed tumors, the latent period being 9 to 25 months (the latent period for 8 of the tumours was about 12 months). The author states: " As would be expected, the tumors varied greatly in microscopic appearance. Some contained much collagen and were composed of spindle-shaped cells of uniform size and appearance arranged in interlacing bundles and whorls. Others were more pleomorphic, with many cells of irregular size and shape, numerous giant cells, abundant mitoses, and less collagen. One tumor was extremely anaplastic, consisting of large, rounded, or polyhedral cells. This was presumed to be a mesothelioma. The others were fibrosarcomas. In many tumors, globules of the injected oil were seen. . . . In the light of present evidence . . . the best interpretation of the carcinogenic action of injected wheat germ oil is that the reaction is a non-specific one to chronic irritation. The production of tumors by overheated oils is presumably a result of the same mechanism ". *I. Hieger*

1786. **Production of Sarcoma in Rats with Light Green SF**
P. N. HARRIS. *Cancer Research* [*Cancer Res.*] **7**, 35–36, Jan., 1947. 2 figs., 2 refs.

Subcutaneous injections of an aqueous solution of light green SF of doubtful purity were given to 30 rats. Of the 25 which survived more than 35 weeks after each

rat had received 1·7 g. of the dye, 15 finally developed tumours at the site of injection (latent period 35 to 85 weeks). The author states that "all tumors were fairly well circumscribed and rounded, and consisted of slightly translucent, whorled gray tissue. Most of the tumours grew rapidly after they became manifest. Microscopically, the tumors were fairly uniform and consisted of fusiform cells arranged in whorls and interlacing bundles. Mitoses were numerous in most tumors, and in only a few were giant cells at all common, although nearly all tumors contained some. Although some cells in a few of the tumors superficially resembled smooth muscle cells, no myofibrillae could be demonstrated, and all tumors were classed as fibrosarcoma".

I. Hieger

1787. **Spontaneous Neoplasms in Fishes. I. Osteochondroma in the Jewelfish, *Hemichromis bimaculatus***
R. F. NIGRELLI and M. GORDON. *Zoologica* [*Zoologica, N.Y.*] **31**, 89–92, Aug., 1946. 14 figs., 4 refs.

Only 4 chondromata in fishes appear to have been recorded before, and no histological descriptions of these have been given. One male out of 100 aquarium-bred jewel fish developed a tumour at the anterior edge of the right operculum, which in 2 months' growth measured 13×6×4 mm. and involved all the small bones of the region. It was smooth and the overlying epithelium was intact. Another small nodule, possibly a metastasis, was found on a gill-raker of the same side. The tumour was vascular and consisted mainly of cartilage with areas of uncalcified osteoid tissue. The transition of subperiosteal cells into chondrocytes was traced. The cartilage cells were irregular in shape and size. Intercellular substance was abundant and some cells were multinucleated, though no mitoses were seen. This structure resembles closely that of some tumours in man. A previous injury is suggested as a possible cause for the condition.

[This scientific name corresponds with the "red cichlid" which is No. 191 in Vol. III of the Vertebrate List of the Zoological Society of London (E. G. Boulenger, 1929). Other tumours of bone and cartilage in fishes are reviewed by Haddow and Blake (*J. Path. Bact.*, 1933, **36**, 41).] *R. E. Rewell*

1788. **Some Effects of Aromatic Hydrocarbons on Sulfur Metabolism and Tumor Induction in Mice**
H. G. CRABTREE. *Cancer Research* [*Cancer Res.*] **6**, 553–559, Oct., 1946. 2 figs., 18 refs.

Two carcinogenic hydrocarbons (3,4-benzpyrene and 1,2,5,6-dibenzanthracene) when painted on the skin of mice had little effect on the urinary sulphur excretion. Four non-carcinogenic hydrocarbons (benzene, naphthalene, phenanthrene, anthracene) caused considerable changes in urinary sulphur excretion indicating mercapturate formation. The author states: "Three possible deductions may be drawn from the data presented: (*a*) The carcinogens do not utilize sulfur by mercapturate formation during their elimination. (*b*) They use sulfur at too slow a rate to permit certain detection by analyses of urine. (*c*) Detoxication mechanisms involving sulfur lead to their excretion by a route different from that used by the hydrocarbons of lower molecular weight. All these possibilities emphasize differences in the behaviour of the carcinogenic and noncarcinogenic hydrocarbons used. But the results do not provide final proof that sulfur does not play a role in the detoxication of carcinogens".

Glutathione estimation of the skin of mice painted with these six hydrocarbons pointed to a similar conclusion. "There is an exact parallelism between these results and those obtained for urinary sulfur partition. They indicate that the known mercapturate formers—naphthalene, anthracene, and phenanthrene—can be detoxicated in the skin. Again, the different behaviour of the 2 carcinogens is noteworthy. No indication is given that sulfur is concerned in their passage through the skin . . ."

Addition of a non-carcinogenic hydrocarbon to a solution of carcinogenic hydrocarbon lowered the potency (prolongation of latent period) suggesting that the carcinogenic mechanism does, after all, involve sulphydryl compounds in the tissues. "All the work on the retardation of tumor induction by inhibitors of sulfu metabolism indicates a direct association between sulfur-containing cell constituents and carcinogens during the primary phases of carcinogenesis. This is fortified by the demonstration, recorded here, that mercapturate-forming hydrocarbons oppose the biological action of the carcinogenic hydrocarbons. Direct evidence for this hypothetical process is not yet available. The metabolic transformations of carcinogenic hydrocarbons so far recorded are all of an oxidative character, and seem to be concerned with processes of elimination, though intermediate phases of these detoxication reactions may well be the true initiators of carcinogenic action. Sulfur conceivably plays a role in the fixation of any such potent derivatives within the cells as a preliminary to the biological changes that culminate in malignant transformation".

I. Hieger

1789. **Stimulation and Retardation of Neoplastic Growth by Sulfhydryl Compounds**
A. BRUNSCHWIG, J. ARNOLD, and J. EDGCOMB. *Cancer Research* [*Cancer Res.*] **6**, 560–562, Oct., 1946. 6 refs.

The author state that "the importance of the sulfhydryl radical (−SH) in intracellular enzyme systems, especially those associated with growth and reaction to injury, has long been recognized. Experiments were carried out to determine if the addition of −SH might stimulate growth of a transplantable rat tumour, and, conversely, if retardation of growth is observed when −SH already present is inactivated by certain agents such as iodoacetic and maleic acids. . . . Since the rate of growth of transplantable neoplasms varies widely among individual rats and appears to be influenced by temperature, diet, and season, these factors were controlled. For each group of experimental animals a parallel control series was maintained in an adjacent cage. . . . Three preliminary control experiments were carried out using a total of 31 rats. Each experiment

consisted of maintaining 3 to 6 rats with tumour transplants in adjacent cages for 2 weeks, and at the end of this period the tumours were excised and weighed. The three groups with the heavier average tumour weights were compared with the three groups of lighter tumour weight. The difference was 16·5%, hence it was assumed that variation in weight in the experiments should exceed 20% to be interpreted as significant ". [The choice of controls must have presented serious difficulties since the average weights of control tumours varied in different groups from 1·82 to 20 g.]

The stimulating effect of some of the —SH compounds was not significant; neutralization tests with anti-SH compounds were not altogether conclusive. The experiments showed that sodium thioglycollate stimulates growth by 30% (the average weight of tumours in the control animals was 4·6 g. and in the treated animals 6·7 g.), disodium thiomalate stimulates by 36%, and sodium thiolactate by 13·5% (not significant). Methionine inhibits tumour growth by 5·5% in small doses and by 19% in larger doses. Cysteine stimulates growth by 12·7% and cystine by 9%. Sodium iodoacetate inhibits growth by 32%, and disodium malate also has a powerful inhibiting effect (44%). In the neutralization experiments sodium thiolactate and sodium iodoacetate given together inhibited growth by 36%, as was expected, since thiolactate did not stimulate. On the other hand, when sodium thioglycollate, a stimulator, and sodium iodoacetate were injected together their effects cancelled each other out, and the resulting growth did not exceed that in the controls to a significant degree. *I. Hieger*

1790. **Effect of Fresh Milk on the Production of Hepatic Tumors in Rats by Dimethylaminoazobenzene**
C. HOCH-LIGETI. *Cancer Research* [*Cancer Res.*] **6**, 563–573, Oct., 1946. 5 figs., 27 refs.

The object of the experiments was to determine the effect of fresh milk on the production of tumours in rats by *p*-dimethylaminoazobenzene.

Diet	Duration of treatment: range in days	No. of animals	Fatty change	Nodular cirrhosis	Cholangiofibrosis	Cholangioma	Hepatoma
Rice + *p*-DA*	73–267	13	6 (46%)	5 (39%)	4 (39%)	11 (85%)	2 (15%)
Rice + casein + *p*-DA.	100–333	19	9 (46%)	9 (46%)	10 (53%)	15 (79%)	6 (32%)
Rice + milk + *p*-DA.	72–465	34	8 (24%)	0	1 (3%)	2 (6%)	0
Rice + milk + *p*-DA.	78–388	22	7 (32%)	0	3 (14%)	3 (14%)	1 (4·5%)

* *p*-DA = *p*-dimethylaminoazobenzene.

" On the 218th day in one animal on a diet of rice, 6% casein, and *p*-dimethylaminoazobenzene, extensive papillomatosis of the forestomach was found, and subsequently this condition was encountered here in 6 out of 6 animals on *p*-dimethylaminoazobenzene. But it was found also in 2 out of 3 rats receiving azobenzene, and in 2 out of 5 control rats. The diameter of the papillomas ranged from 0·2 to 5 mm.; they were not ulcerated. Microscopically, extensive hyperkeratosis and benign hyperplasia of the squamous epithelium were found. Only in 1 case, an animal on casein–rice diet with *p*-dimethylaminoazobenzene, was there any sign of downgrowth and penetration of the muscularis mucosae ".

The author refrains from final generalizations on the consumption, and therefore possible protective action, of fresh milk by those human races particularly liable to liver cancer. He states: " The data collected by Berman (*S. Afr. J. med. Sci.*, 1940, **5**, 54) indicate that primary cancer of the liver is prevalent in varying degree over the southern half of Africa, India, the East Indies, China, and Japan. The published material yields the following figures for primary carcinoma of the liver as a percentage of carcinoma of all organs:

	%		%
Bantu	37	Philippines ..	22
Javanese	36	Semi-Bantu ..	18·7
Chinese	36	Japanese	7·8
Indians	28		

Over this vast area there is of course an immense variety of dietetic conditions and habits, about which it is difficult to collect complete information and impossible to generalize at present. It seems unlikely that any single positive factor, that is, the same carcinogenic substance in the food, operates over so many different countries, though such a factor may be present in some areas; for example, Portuguese East Africa. A deficiency in the diet is more likely to be common to all these peoples, and this deficiency might be one that is made good by some constituent of milk ".

I. Hieger

1791. **Experimental Medionecrosis of the Aorta**
J. G. SCHLICHTER. *Archives of Pathology* [*Arch. Path.*] **42**, 182–192, Aug., 1946. 8 figs., 97 refs.

Medionecrosis of the aorta, with occasional aneurysm formation, can be produced easily and by a variety of methods in the rabbit, but in dogs only with great difficulty and by one method—the injection of sublethal doses of histamine. The author produced ischaemia of the media of the ascending aorta in dogs by cauterizing an area of 2 sq. cm. in a region in which the vasa from the two coronary arteries and the brachiocephalic vessels of the arch anastomose. Seven normal dogs and one with hypertension were used, and killed at intervals from 6 hours to 6 weeks after cauterization. Up to 12 hours the only changes in the media were oedema of the inner third and haemorrhages in the outer third. From 1 week onwards the pericardium and right auricle were adherent to the aorta. At 1 week there was diffuse necrosis of the outer two-thirds of the media, beneath the cauterized area and for some distance beyond it, though islands of normal media remained

beneath the cauterized area. From the second week onwards necrosis proceeded, affecting the elastic fibres, and concurrently repair started, granulation and young fibrous tissue appearing; during this period intimal proliferation was marked. Later healing was by the formation of fibrous tissue. In 1 dog the whole aortic wall became necrotic; a rupture of the intima occurred and produced a dissecting aneurysm.

Medionecrosis appears to be caused by ischaemia of the aortic wall. In rabbits the blood supply is poor, and hence even slight interference with it is effective; but in dogs the blood supply is rich, with many anastomoses, so that medionecrosis can be produced only with difficulty. The blood supply of the aortic wall of man appears to be intermediate between that of rabbit and dog. Healing of the lesions depends on the adequacy of the collateral circulation, which is extremely variable in the ascending aorta. *G. Discombe*

1792. **The Erythrocyte Sedimentation Rate in the Cerebrospinal Fluid.** (La velocità di eritrosedimentazione nel liquor cefalorachidiano)
V. Giunti and E. Rottini. *Giornale di Clinica Medica* [*G. Clin. med.*] **27**, 536–543, July, 1946. 10 refs.

Of the numerous factors affecting both erythrocyte sedimentation rate (E.S.R.) and flocculation reactions (such as the Takata-Ara), probably the most important is the total and relative amounts of the proteins in the fluid. Many investigations have been made to determine the relation between the E.S.R. in different normal and pathological body fluids, and also to correlate the E.S.R. and the flocculation reaction in the same fluid. Garnier and Oumansky carried out sedimentation-rate tests with washed red cells suspended in citrated pleural and peritoneal fluids. Inflammatory exudates, richer in albumin, gave higher figures than transudates, and there was some degree of correspondence between E.S.R. and albumin content. Washed red cells from different subjects gave varying results when suspended in the same fluid, showing that the cells play a part in determining the E.S.R. Cohen *et al.* showed that the E.S.R. increases progressively in ascitic fluid from cases of hepatic cirrhosis, pleural transudates from cases of circulatory failure, pleural effusion following pneumothorax, serous tuberculous effusion, and tuberculous empyema.

The authors used the following technique to investigate the E.S.R. in cerebrospinal fluid, and to determine the relation between it and the standard flocculation reactions (Pandy, Boveri, Nonne-Apelt): Four ml. of fluid obtained by lumbar puncture was mixed with 1 ml. of 3·8% sodium citrate and centrifuged. Six ml. of blood from a vein of the same subject was diluted with 3 ml. citrate; some of this mixture was set up in a 200-mm. Westergren tube. To 2 ml. of the citrated blood was added 2 ml. of citrated cerebrospinal fluid; with another 2 ml. of the blood was mixed an equal quantity of 0·9% saline, and these suspensions were also set up in sedimentation tubes. Four ml. of fresh blood was centrifuged after the addition of 1 ml. of citrate; the supernatant fluid was then removed and replaced by an equal quantity of spinal fluid, and the resultant mixture was allowed to sediment in a Westergren tube. Since in a preliminary experiment it was found that washing the red cells made no significant difference to the results, this was not done in preparing the fourth mixture. At the same time Pandy, Boveri, and Nonne-Apelt tests were done on the cerebrospinal fluid, and in some cases the protein content was estimated.

The following conclusions were reached: There is no relationship between protein content and E.S.R. in the cerebrospinal fluid, or between the E.S.R. of the spinal fluid and blood of the same subject. In acute inflammatory processes of the meninges the E.S.R. in the cerebrospinal fluid is increased without regard to the intensity of the flocculation reactions. In cases of progressive paralysis, notwithstanding the rise of protein and the positive flocculation reactions, the E.S.R. in the cerebrospinal fluid does not become significantly increased. *E. G. Sita-Lumsden*

1793. **Whole-blood Cholinesterase Determinations in Some Hematologic Dyscrasias: Low Cholinesterase Values in the Leucoses**
R. D. Barnard, H. Sprinz, H. M. Fitch, R. A. Lehman, and R. A. Walker. *Science* [*Science*] **104**, 449, Nov. 8, 1946.

Whole-blood cholinesterase determinations were made in 14 cases of leukaemia, comprising 7 cases of acute or subacute " myeloblastosis ", 1 of acute " monoblastosis ", 1 of acute " lymphoblastosis ", 4 of chronic " myeloblastosis ", and 1 of chronic lymphatic leukaemia. With the exception of the last case, all showed a reduction in the blood cholinesterase proportional to acuteness and clinical severity, but not to erythrocyte or leucocyte counts. The cholinesterase values were normal in 14 cases of various non-leukaemic haematological conditions, but they were reduced in all of 3 cases of macrocytic anaemia and elevated in 1 of 3 cases of polycythaemia vera. It is suggested that the asthenia and extreme pallor attending acute leucoblastosis may result from profound cholinergic intoxication which produces an " irreversible shock state characteristized by the atopic-exudative syndrome of thrombocytopenic purpura. The last phase is usually not accounted for on the basis of myelophthisis or leucoblastic infiltration ".

[There is surely ample evidence that extensive leucoblastic infiltration of the bone marrow is invariably present in the terminal stages of acute leukaemia.]
L. J. Davis

1794. **New Westergren Technique**
E. H. Hudson. *British Medical Journal* [*Brit. med. J.*] **1**, 93, Jan. 18, 1947.

1795. **The Preparation and Use of Colloidal Gold Sols as Diagnostic Agents**
N. F. Maclagan. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **27**, 369–377, Dec., 1946. 20 refs.

Microbiology

1796. **Chemical Studies on Host-virus Interactions. II. The Chemical Simulation of the Interference Phenomenon by 5-Methyl Tryptophane**

S. S. COHEN and T. F. ANDERSON. *Journal of Experimental Medicine* [*J. exp. Med.*] **84**, 525–533, Nov., 1946. 3 figs., 6 refs.

The authors describe an attempt " to inhibit virus multiplication by chemical means in a manner approximating the observed conditions of the interference effect ". The studies were carried out on *Bacterium coli* B and phages T2 and T4, because, as indicated by the authors in a previous paper, the use of bacteria and appropriate phages permits study and control of the reaction of host and parasite in known numbers and conditions, with relative ease of assay. Inhibition of host multiplication does not necessarily result in interference with virus multiplication. On the other hand, common respiratory poisons might be expected to prevent virus multiplication in addition to their other effects. To simulate interference an inhibitory compound which does not grossly affect the rate of oxygen utilized and the respiratory quotient is necessary. The compound tested was 5-methyl tryptophane (5 MT). A synthetic medium " F " containing 10 g. sodium lactate, 1 g. ammonium chloride, 0·7 g. dipotassium hydrogen phosphate, 0·3 g. potassium dihydrogen phosphate, 0·01 g. magnesium sulphate, 0·1 g. sodium sulphate per litre of distilled water was employed.

A bacteriostatic concentration of 5 MT did not kill the *B. coli* or the bacteriophages employed when tested separately. The number of bacteria necessary for estimation of oxygen consumption is approximately 10^9. Concentrations of 5 MT of 460 micromols per litre were bacteriostatic for approximately 4 hours; 4·6 micromols per litre were not bacteriostatic at all. The final phage titre in *coli* systems infected in the presence of 460 micromols of 5 MT per litre was 1/100 to 1/1,000 of that found in the absence of this substance. Virus multiplication in concentrated bacterial suspensions as here employed does not follow the normal course, there being a relative absence of " bursts " and lysis; the amount of virus found by the plaque method seldom exceeds the amount added. Hence these experiments only indicate a loss of virus in the presence of 5 MT, whereas there was no significant diminution of phage or bacteria alone when incubated in the presence of the drug.

To demonstrate failure of virus multiplication a 2,000-fold dilution of a 10^8 per ml. bacterial suspension infected with virus was first made. New virus was liberated in a burst. Then tests of such dilute suspensions with phage T4 and 460 micromols 5 MT per litre were carried out. Tryptophane replaced 5 MT in a control test, because it has been found essential as a co-factor for adsorption on the *coli* strain. Serial assays on nutrient agar showed a continuous fall in the number of infectious centres over a period of 2 hours, while the control, following a constant period, showed a steep rise after 30 minutes (corresponding to the " burst ", the size of which by calculation was found to be 70). This rise lasted for about 40 minutes and was followed by another constant period. Tests of phage T2 (without tryptophane in the control, because co-factor is unnecessary for this phage) gave a similar result, though the fall in infectious centres in the test was more marked.

With *B. coli* there are three phenomena under the conditions of the interference effect induced by two phages; (1) inhibition of multiplication of subsequently added virus; (2) inhibition of multiplication of host; and (3) no apparent change in the oxygen utilization of the host. In sufficient concentration 5 MT produces all three characteristics. Two-phage interference effects on the host are irreversible; the effects of 5 MT are reversible. *G. T. L. Archer*

1797. **The Antibiotic Effect *in vitro* of Quinones on Staphylococci, *C. diphtheriae* and *S. typhi*.** (Sull'attività *in vitro* di alcuni chinoni (chinidrone, benzochinone) di fronte allo stafilococco, al bacillo difterico e al bacillo del tifo)

L. NASSI. *Bollettino della Società Italiana di Biologia Sperimentale* [*Boll. Soc. ital. Biol. sper.*] **22**, 139–141, March, 1946. 2 refs.

The structure and nature of penicillin and of its active constituents have been studied by several workers. There are indications that the latter are allied to the quinone group, present in aspergilli as well as in penicillia. The author has therefore studied the antibiotic action of certain quinone derivatives on *Staphylococcus aureus*; on *Corynebacterium diphtheriae* (a strain isolated from the throat of a child with severe faucial diphtheria, the test being carried out on a surface growth of a suspension of the organism in saline on Pergola's medium); and on *Salmonella typhi*. The members of the quinone group tried on the staphylococcus were hydroquinone, quinhydrone, and benzoquinone; the two last were tried on the other organisms. The procedure was as follows. In each plate, after the sowing, small pockets were made with a borer of 6 mm. diameter, each capable of holding 0·1 ml. In these pockets were placed the dilutions of the chemical substances, and readings were taken after the plates had been in the thermostat for 24 and 48 hours. For the staphylococcus and *S. typhi*, dilutions ranged between 0·08 and 0·000008%, for *C. diphtheriae* from 0·2 to 0·0002%.

The antibiotic activity of benzoquinone and quinhydrone was about the same towards the staphylococcus, against which they were effective at a concentration of 0·004%, and *C. diphtheriae*, against which they were effective at a concentration of 0·002%. With the former organism the hydroquinone acted at the same

concentration, 0·004%. With *S. typhi* the two quinones were equally effective at a concentration of 0·04%.

Assuming that 0·002 mg. of penicillin contains 0·8 Oxford unit, it may be said that benzoquinone and quinhydrone had an antibiotic action in amounts corresponding to 0·8 Oxford unit in respect of *C. diphtheriae* and to 1·6 Oxford units in respect of staphylococcus. In the case of the more resistant typhoid organism, the effective antibiotic dose was 16 Oxford units.

[These *in vitro* findings are to be applied *in vivo*, but a point to be borne in mind is the " coefficient of toxicity " for man of some of the quinone group; benzoquinone in particular has a high coefficient.]

H. Harold Scott

1798. **The Antibiotic Effect *in vitro* of Naphthoquinones and of Synthetic Water-soluble Vitamin K on Staphylococci, *C. diphtheriae*, and *S. typhi*.** (Sull'azione antibiotica, *in vitro*, di sostanze naftochinoniche e della vitamin K sintetica, idrosulubile, verso lo stafilococco, il bacillo difterico e il bacillo del tifo)

L. Nassi. *Bollettino della Società Italiana di Biologia Sperimentale* [*Boll. Soc. ital. Biol. sper.*] **22**, 141–144, March, 1946. 1 ref.

The author has studied the antibiotic action of naphthoquinone and of a number of related compounds. Naphthoquinone is poorly soluble in water, more soluble in alkalies, and completely soluble in oils. For his experiments he has used 0·04% solutions in water for all three organisms, *Staphylococcus aureus*, *Corynebacterium diphtheriae*, and *Salmonella typhi*, and, for the first-named, 0·08% alkaline and oily solutions. He tested with these strengths, undiluted and in dilutions up to 1 in 1,000.

The results were: effective action on the staphylococcus in a 1 in 2 dilution of all solutions and a partially effective action with the watery solution diluted 1 in 4. The watery solution acted on *C. diphtheriae* in dilutions up to 1 in 20 and on *S. typhi* up to 1 in 4. In other words, this compound has an antibiotic effect in a dose of 0·0004 mg., equivalent to 0·16 Oxford unit of penicillin (each mg. of penicillin corresponding to 400 Oxford units). It is less toxic than benzoquinone and, *in vitro* at least, is almost as active as penicillin itself. It is, therefore, more effective than benzoquinone against the typhoid organism—a remarkable fact in that this bacterium is penicillin-resistant.

In another series of experiments the author tested a sulphonamide compound of naphthoquinone and also its sodium salt. Neither had any antibiotic action in the various concentrations tried on any of the three organisms, In yet another series he used a preparation of vitamin K—2-methyl-1-4-disuccinyl-naphthoquinone —in 1% solution and in dilutions from 1 in 2 up to 1 in 100. Against *Staph. aureus* it was active up to 1 in 20, against *C. diphtheriae* to 1 in 10, against *S. typhi* to 1 in 2 and partially 1 in 4. Methyl-naphthoquinone is relatively of low toxicity; a rabbit tolerates a dose of 30 mg. per kilo body weight; in man a dose of 3 mg. per kilo, or 180 to 200 mg. a day, may be given before toxic symptoms—vomiting, epigastric pain, albuminuria, and porphyrinuria—arise. *H. Harold Scott*

1799. **A New Method of Differentiating *C. diphtheriae* from other Corynebacteria.** (Nuovo metodo per la differenziazione del corinebatterio della difterite dagli altri corinebatteri ad esso simili)

G. Lissia. *Bollettino della Società Italiana di Biologia Sperimentale* [*Boll. Soc. ital. Biol. sper.*] **22**, 329–331, April, 1946.

Having observed that true *C. diphtheriae* acidifies the medium in which it is growing, whereas with " diphtheroids " the medium becomes alkaline or keeps its *p*H unchanged, the author has devised a medium in which this fact is utilized for distinguishing *C. diphtheriae* from organisms resembling it. He was led to consider the matter because he had a case of diphtheria of the vulva in a child of 7 months. Bacteriological examination showed that the organism isolated had all the morphological characters of the Klebs-Löffler bacillus, but the biological tests were negative. Inoculation into guinea-pigs gave rise to fever and local oedema, but was not fatal; when the animals were killed, however, they showed all the signs associated with inoculation with the true *C. diphtheriae*. Administration of antitoxin speedily cleared up the lesion in the child.

The method recommended is a modification of the ordinary Löffler's medium; human serum, inactivated by heating to 56° C. for half an hour, is substituted for the ox-serum, the glucose is omitted, and 4 drops of 0·4% alcoholic solution of brom-methyl blue is added. The tube, after being inoculated, is placed in the incubator in a sloping position so that the surface is bathed in the water of condensation. In 4 hours the colour changes to yellow with true *C. diphtheriae*, whereas diphtheroids leave the blue unchanged or darken it somewhat. If broth is used for the culture 4 drops of the indicator is added to 100 ml. of the medium; the change in colour, either to yellow or darker blue, is visible after 10 to 15 hours at 37° C. *H. Harold Scott*

1800. **Effect of Metal Chlorides of the Second Group in Periodic Table on various Micro-organisms.** (Über die Wirkung der Metallchloride der zweiten Gruppe des periodischen Systems auf verschiedene Mikroorganismen)

R. Koulumies. *Acta Pathologica et Microbiologica Scandinavica* [*Acta path. microbiol. scand.*] Suppl. 64, 1–99, 1946. 29 figs., 111 refs.

The author has examined the bactericidal action of chlorides of metals of the second group in the periodic table of elements. In his first method suspensions of the organisms were exposed to solutions of the metal salts, and the resulting viability was estimated by subcultures on standard media. In the second method the organisms were grown on standard media in which the chlorides were incorporated. The organisms included some 83 strains, with some anaerobes, *Mycobacterium tuberculosis*, and fungi.

The diagrams accompanying the article show that the chlorides can be arranged in a toxicity sequence, such that calcium and magnesium are less toxic than strontium, and strontium less than barium, and so on through beryllium, zinc, and cadmium to mercury. The sequence is similar to that found by other workers by animal

experiments. The earlier opinion that the toxicity of metals rises with increase in their atomic weight is, with few exceptions, confirmed by the present results. But the rule does not apply to the metals of alkaline earths of the group, for the lightest of them, beryllium, is usually the most toxic. Indeed the uniformity of the bacteriostatic figures obtained with that element gives the author reason to believe that beryllium is well suited for such experiments on bacteria. The other extreme is found with cadmium chloride.

The influence of metallic chlorides on bacteria depends much on their species; with different strains of the same species differences were found with only two, *Pasteurella* and *Pneumococcus*. A striking selective difference was seen when it was shown that *Corynebacterium pseudodiphtheriae* is four times as susceptible to strontium chloride added to McLeod's medium as is *C. diphtheriae*. *Vibrio cholerae* strains were six times more resistant to cadmium than was *Bacterium coli*. Strains of *M. tuberculosis* showed much greater susceptibility to barium incorporated with Löwenstein's medium than did any other bacteria examined; yet, when a barium solution was used for its direct action it failed to kill in 24 hours. Leptospirae were found exceedingly susceptible to chloride of mercury.

R. G. Bannerman

1801. **Studies on the Relative Resistance of Germs to the Salts of Metals of Group I of the Periodic Table.** [In English]
A. R. ALHA. *Acta Pathologica et Microbiologia Scandinavica* [*Acta path. microbiol. scand.*] Suppl. 65, 1–74. 1946. 129 refs.

This monograph contains a large mass of data which cannot be summarized adequately; the original should be consulted by those interested in the subject. A review of the literature is included. The author investigated the bacteriostatic and bactericidal properties of lithium, sodium, potassium (and ammonium), rubidium, caesium, copper, silver, and gold against a wide and representative range of bacteria and moulds. The chlorides of each element were used except for the nitrate of silver. For each element and organism an estimate was made of the highest molar concentration of the salt incorporated in the medium that would allow growth. Many of the salts combined chemically with constituents in the media, and therefore for a number of organisms bactericidal tests were carried out. The suspensions of the organism were added to varying dilutions of solutions of the salt, and subcultures were made after 1, 5, and 60 minutes, and after 24 hours. No attempt was made to neutralize the chemical present in the inoculum subcultured.

There was little difference in the bacteriostatic tests between the alkali metals, except that caesium was considerably more toxic. The heavy metals also had a higher range of toxicity. For most organisms the order of increasing bacteriostatic power was copper, gold, silver; for the tubercle bacillus copper was the most bacteriostatic. In the bactericidal tests sodium chloride showed no lethal action; the other alkali metals killed bacteria in saturated solutions only after prolonged contact. Caesium, in spite of its relatively high bacteriostatic action, had a low bactericidal power. Solutions of the heavy metals appeared bactericidal in weaker concentrations than were inhibitory in the bacteriostatic tests, where their action was probably interfered with by chemical combinations with constituents in the media. Copper salts were bactericidal only after prolonged contact; only strong concentrations were effective within 1 or 2 minutes.

The different organisms varied considerably in their sensitivity to the metallic salts. The fungi were very resistant. *Leptospira icterohaemorrhagiae* was the most susceptible, followed by the Gram-negative cocci, pneumococci, and streptococci. Particular sensitivities of certain bacteria to certain metals were noted. *L. icterohaemorrhagiae* was very susceptible to gold, and the tubercle bacillus was relatively more sensitive to the alkali metals and copper. On the other hand, *Corynebacterium diphtheriae* was relatively resistant to the alkali metals, except caesium, and to copper. In the bactericidal tests the tubercle bacillus was particularly difficult to kill. The author suggests a few possible practical applications from these results. Lithium and copper might with advantage be incorporated in selective media for *C. diphtheriae*. The resistance of fungi to silver and gold might be applied to their isolation. Caesium, which has a low toxicity for animals, might be tried as a chemotherapeutic. *Streptococcus viridans* differs from *Str. pyogenes* in its greater resistance to copper. The action of caesium raises problems of theoretical interest. It has a fairly high bacteriostatic action against all bacteria, yet in solution its bactericidal power is negligible. It differs from the heavy metals in that its sulphide is soluble and so it cannot act by combining with the —SH grouping. It does not appear to form insoluble albuminates.

D. G. ff. Edward

1802. **Bactericidal Power of Electrolytic Hypochlorite**
R. F. MILTON and J. L. HOSKINS. *Nature* [*Nature, Lond.*] **158**, 673, Nov. 9, 1946. 1 ref.

The authors suggest that the bactericidal effect of electrolytic hypochlorite (a buffered solution containing hypochlorous acid and sodium hypochlorite) is due to hypochlorous acid rather than to free chlorine, and in support instance an experiment in which the bactericidal effect of chlorine water, commercial sodium hypochlorite, and electrolytic hypochlorite were compared, using *Bacterium coli* as the test organism. Electrolytic hypochlorite appeared to have a somewhat more rapid effect than the other two.

C. L. Oakley

1803. **The Nucleic Acid and Carbohydrate of Influenza Virus**
C. A. KNIGHT. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 99–116, Jan. 1, 1947. 3 figs., 37 refs.

Both ribonucleic and desoxyribonucleic acids have been obtained from purified particles of PR8 influenza virus derived from infected allantoic fluid. These particles were found also to contain carbohydrate additional to that of the nucleic acids. Carbohydrate-rich fractions, essentially devoid of nucleic acid, were obtained from

PR8 and Lee strains. It seemed reasonable to conclude that the particles contain a polysaccharide composed of mannose, galactose, and glucosamine units.

Previous work by the author with the precipitation technique (*J. exp. Med.*, 1946, **83**, 281) suggested that the particles of PR8 and Lee viruses in allantoic fluid contained a minimum of 20 to 30% respectively of antigen characteristic of "sedimentable protein" of normal allantoic fluid. In this present study it has appeared that the amount of normal antigen in the most highly purified virus-containing particles can be ascertained from the glucosamine content. Such calculations suggest that the particles of Lee and PR8 viruses contain about 78 and 59% respectively of host antigen; these values are considerably above those indicated by precipitin tests. These values, however, rest on the assumption that glucosamine is absent in the portion of virus particle unrelated to the host. At present this is speculative.

A. J. Rhodes

1804. **Staphylococcal Antitoxin Reaction in 368 Patients.** (Stafylococantitoxinreaktion hos 368 Patienter)
M. KNUDSEN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **108**, 1210–1212, Oct. 31, 1946. 3 refs.

The author reports on 368 suspected cases of extrapulmonary tuberculosis admitted to Juelsminde hospital for observation between Jan. 1, 1943 and June 1, 1945, in all of which the titre of staphylococcal antitoxin in the serum was determined as an aid to diagnosis. Titres of 8 or higher were taken to be pathological, and in such cases estimations were repeated once a month and the results compared with findings of staphylococci in pus, fistular secretions, tissue samples, or swabs. The following correlation was found: values of 8 or higher were obtained in 45 cases (12·1%), and in 20 of these staphylococci were found in the pus. The organism was also found in the pus in 28 cases in which the titre was below 8, but of the 298 cases in which no staphylococci were found only 18 (6%) had a titre of 8 or higher. No significance is attached to a further 22 cases in which staphylococci were found in the fauces. Of the 321 cases (87%) finally diagnosed as cases of tuberculosis, 150 were of the open and 171 of the closed form of the disease; 16·3% of the former and 6·2% of the latter had titres of 8 or higher. In 27 of the 45 cases of high titre a staphylococcal focus was discovered and the titre fell to the normal level when it had been eliminated. The author does not consider, however, that the value of the titre can be taken as a measure of the severity of the infection. He concludes that the staphylococcal antitoxin reaction may be of diagnostic value, but draws attention to the danger of attaching undue importance to a reaction based upon such widely occurring bacteria as the staphylococci.

B. Nordin

1805. **A New Selective Medium for the Isolation of Salmonellae from Stools**
O. FELSENFELD and V. M. YOUNG. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **17**, 13–15, Jan., 1947. 10 refs.

1806. **Immunity to Anthrax: Protective Antigen Present in Cell-free Culture Filtrates**
G. P. GLADSTONE. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **27**, 394–418, Dec., 1946. 35 refs.

An attempt was made to obtain from culture filtrates of *Bacillus anthracis* an antigen similar to that which has been found on numerous occasions in anthrax oedema fluid. Attempts to produce this antigen with media containing such substances as filtered extracts of rabbit organs, muscle and skin, leucocytes and red cells, and oedema fluid obtained by injection of turpentine and *B. anthracis* were unsuccessful; but the antigen was found in filtrates of cultures grown in coagulated rabbit plasma. The culture was reaped at different times of growth, the clot being broken up, allowed to contract, and the serum filtered through a Seitz filter. These filtrates were highly active, complete protection being obtained in rabbits after 3 weekly doses of 1·0 ml. The size of culture inoculum was important, an inoculum of 10^8 spores or greater giving little or no antigen. The culture had to be reaped at the correct time, the antigen being destroyed after 48 hours. It was found that a *p*H between 6·96 and 8·43 was required. Similar cultures with guinea-pig, human, sheep, and horse plasmas were tested and filtrates were all active. The bulk of the work was done with sheep plasma culture filtrates. Sheep P.C.F. in 3 weekly doses of 1·0 ml. protected rabbits against 1,000, 10,000, and 100,000 A.L.D. of *B. anthracis* spores. In addition to tests on rabbits, P.C.F. from various plasmas was tried in protection tests on guinea-pigs, mice, sheep, and monkeys. Sheep and monkeys were protected; guinea-pigs and mice were not, though guinea-pigs showed prolonged survival time.

P.C.F. was shown to be non-toxic and to be destroyed by heating at 60° C. for 1½ hours. After 180 days in the ice-chest (+1° C.) there was no significant fall in activity if *p*H was between 5·95 and 8·76. It appears that the antigen is produced extracellularly. Various strains of *B. anthracis* were used, and it was found that the production of antigen had no relation to the degree of virulence, capsulation, or sporulation of the strains. No virulent strain failed to yield antigen, and the formation of antigen by avirulent strains was related to their efficiency as living vaccines. No antigen was produced by *Bacillus cereus*. The antigen could also be obtained from cultures in sheep serum, and in rabbit serum if a small amount of agar was added to the latter. An analysis of the culture medium, plasma or serum, was made to determine the constituents responsible for the production of P.C.F. Two factors were found to be necessary. One is dialysable and can be replaced by sodium bicarbonate. The other is retained and is a serum protein or associated with it, probably albumin; the author considers it possible that the antigen is formed from normal serum albumin by coupling of an active haptene produced by the organism. Sera from rabbits and sheep hyperimmunized with the antigen contained no protective antibodies, nor could protective antibodies be demonstrated when the spleen, liver, or bone marrow

of immune rabbits was ground up in their serum. Further immunization of such animals with living virulent bacilli produced effective protective sera, but the protective antibodies from such were not absorbed with the antigen from culture filtrates, or with living bacilli. *In vitro* tests were similarly negative: sera from animals hyperimmunized with P.C.F. and living organisms, when tested against sheep and rabbit P.C.F., gave no precipitation or complement-fixation reactions. *T. D. M. Martin*

1807. **Lipid Haemagglutinins**

J. D. STONE. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **24**, 197–205, Sept., 1946. 9 refs.

Tissue extracts containing lipoids agglutinate the same range of red blood corpuscles as vaccinia and ectromelia virus agglutinins. Attempts to isolate the agglutinating principle from tissues have been unsuccessful, and the agglutinating effect of various purified lipoids has been investigated as a means of identifying the haemagglutinins of animal tissues. Cholesterol and ergosterol showed a slight haemagglutinating activity, but that of phospholipoids was much higher. Cephalin showed a haemagglutinating titre of 10^6; this increased on storage, suggesting that the active agent may be an oxidation product. Lecithin had a titre of 10^4. Other figures obtained were: lysocephalin, 2×10^4; lysolecithin, 4×10^4; sphingomyelin, $2{\cdot}5\times10^5$; cardiolipin, 10^6 (susceptible fowl cells) and 8×10^4 (insusceptible fowl cells). No one lipoid was found to give results comparable with those obtained with tissue extracts, and mixtures of lipoids were then tried. These gave higher titres (cholesterol + lecithin, $9{\cdot}6\times10^6$; lecithin + cardiolipin, 10^7; sphingomyelin + cholesterol, $3{\cdot}2\times10^6$) but only when the original alcoholic mixture was diluted with saline, which seemed to be an essential step in the production of a higher titre. The mixture also showed an increased titre when cholesterol was replaced by ergosterol or maize sterols. It was concluded that the haemagglutinating activity of saline extracts of animal tissues could be paralleled by a mixture of lecithin and cholesterol after dilution with saline. *D. J. Bauer*

1808. **Inactivation of Vaccinia and Ectromelia Virus Haemagglutinins by Lecithinase**

J. D. STONE. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **24**, 191–196, Sept., 1946. 18 refs.

The haemagglutinins associated with vaccinia and ectromelia viruses resemble phospholipoids in their action, and it has been suggested that they consist of a combination of a phospholipoid with specific virus protein. If this is the case, virus haemagglutinin should be inactivated by lecithinase, which breaks down the phospholipoid component. This has been found to be the case in the present work. The α-toxin of *Clostridium welchii* and also cobra venom were used as sources of lecithinase; virus haemagglutinins were used in the form of suspensions of infected chorio-allantoic membranes. When vaccinia haemagglutinin was incubated with enzyme at 37° C. the haemagglutinating titre was reduced almost to zero over a 4-hour period. This effect was lost if the toxin was boiled, or in the presence of antitoxin, and was therefore a specific enzyme action. No inactivating effect was seen in the absence of Ca++ ions, which are necessary for lecithinase activity. Similar results were obtained with ectromelia haemagglutinin, but the haemagglutinin of the Melbourne strain of influenza A virus was not affected by the enzyme. From a knowledge of the range of substrates upon which the enzyme acts it is concluded that the virus haemagglutinins contain a phospholipoid which is probably lecithin or sphingomyelin. *D. J. Bauer*

1809. **On the Standardisation of Haffkine Institute Polyvalent Anti-snake-venom Serum against the Venoms of the Four Common Indian Snakes (Cobra, Common Krait, Russell's Viper and Saw-scaled Viper)**

A. K. HAZRA, D. C. LAHIRI, and S. S. SOKHEY. *Bulletin of the Health Organisation* [*Bull. Hlth Org. L. o. N.*] **12**, 384–389, Oct., 1946. 4 figs., 5 refs.

Until recently the anti-snake-venom serum used in India was bivalent and effective only against the venoms of the cobra and Russell's viper. The workers at the Haffkine Institute have now produced a polyvalent serum effective against the four common poisonous snakes of India—cobra, common krait, Russell's viper, and saw-scaled viper. This polyvalent serum is dried from the frozen state in ampoules for use in the field. At the same time the authors have developed a method for the control of potency of the serum by titration against standard venoms. The latter were prepared by pooling more than 100 samples of venom from each of the species of snakes, all the samples having been preserved in the dry state. The reconstituted standard venoms were finally distributed into neutral glass ampoules and re-dried after freezing. For assay purposes 10 mg. of the dried venom is dissolved in 1 ml. of normal saline and the required dilutions are made from this solution. The technique of the actual test is a modification of that described by Ipsen, white mice being used as the experimental animals. Twenty white mice each weighing approximately 20 g. are used for each assay. Mixtures of venom dilutions with ascending proportions of immune serum are allowed to remain in contact for half an hour at 37° C. and then injected into the mice. The animals' response is observed for 2 hours and a final result is recorded after 24 hours. Examples of assays of the polyvalent sera show that 1 ml. will neutralize on an average 0·8 mg. cobra venom, 0·6 mg. krait venom, 0·7 mg. Russell's viper venom, and 0·55 mg. saw-scaled viper venom. The authors state that the results are invariably clear-cut and reproducible within narrow limits. *H. J. Bensted*

1810. **Selection of Salmonella and Shigella Cultures for Serologic Classification**

W. H. EWING and D. W. BRUNER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **17**, 1–12, Jan., 1947. 25 refs.

Paediatrics

1811. **Some Recent Changes in the Outlook for the Child**

F. V. G. SCHOLES. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 617–622, Nov. 2, 1946.

From clinical experience as medical superintendent of Queen's Memorial Infectious Diseases Hospital, Fairfield, Victoria, the author surveys for Australia the major infections of childhood. Apart from the almost stationary death rates in the first week of life, there has been an enormous fall in infant mortality between 1911 and 1941. During this period the reduction in mortality from pneumonia and bronchopneumonia has been only slight; the great saving in infant lives has been due mainly to the decline in the number of deaths from entero-colitis. In 1911 and 1941 the death rates (per 1,000 births) from diarrhoea and enteritis for children under 2 years were 22·8 and 1·5 respectively.

Less striking but still significant is the fall in Australia in deaths from tuberculosis in young children for the same period. In 1911, in children under 5 years, there were 238 deaths; in 1941 the figure was 70. In children between 5 and 10 years the corresponding figures were: 1911, 61 deaths; 1941, 22 deaths. This fall is reflected in the striking results of Mantoux tuberculin tests recently carried out in 1,400 Adelaide schoolchildren by Fry; the percentage of positive reactors in children between 3 and 7 years was 4·1, and in those from 10 to 16 years it was 10·1. The importance of early diagnosis and of removal from the family source of infection is emphasized.

With regard to measles and whooping-cough, in nearly all the fatal cases death is due to complicating bronchopneumonia; the use of sulphadiazine, sulphamerazine, and sulphathiazole has effected "a notable saving of life, more rapid resolution of the lesion in nearly all cases, and a greatly shortened stay in hospital". The limited need for penicillin is discussed. Other complications such as otitis, stomatitis, laryngitis, and pleural empyema can be prevented by the use of sulphonamides and penicillin. Treatment in hospital of cases with the major complications has saved many lives, and preference should be given to them over mild cases of diphtheria and scarlet fever in older children. The respective values of adult and convalescent sera in measles are discussed, and reference is made to the γ-globulin fraction of plasma protein introduced by Cohn in America. The results obtained with this globulin fraction in 116 contact children were better than those obtained with convalescent serum.

As regards diphtheria most deaths are due to the acute primary laryngeal type in young children, to malignant or "missed" severe diphtheria in schoolchildren and young adults, or to neglected laryngo-tracheo-bronchial diphtheria of *mitis* type. The correlation between bacteriological type and severity of illness is not absolute, though the association of *mitis* type with mild laryngo-tracheal infection is characteristic. In epidemics of *gravis* and *intermedius* types large numbers of children may be mildly affected. The severe diphtheria epidemic in Australia in 1941 stimulated a more systematic immunization, and an outbreak among schoolchildren in 1945 of *mitis* type with high mortality showed that immunization in infancy was not a sufficient safeguard. Immunization should begin at 10 months, but re-testing and, if necessary, re-immunization should be done when children enter school. The question of simultaneous immunization against diphtheria and whooping-cough is discussed. Since more than half of the deaths from whooping-cough are among children under 1 year it is suggested that simultaneous immunization should begin at 6 months. In individual cases, however, it may be wiser to immunize for whooping-cough at 3 months and for diphtheria at 6 months.

Streptococcal infection is not a common cause of death in infants, but "from then on, both as a primary and complicating factor, it produces more damage than any other infection, and is dominant in destructive processes in the upper, middle, and lower portions of the respiratory tract". These effects are increased by the low immunity and consequently by frequent re-infection. Streptococcal pharyngitis, with its severe and destructive local complications in the adjoining passages of the nose and ears and its remote effects in nephritis and rheumatism, is, therefore, a major infection and is placed alongside bronchopneumonia. Scarlet fever is "a complication of streptococcal infection", but, apart from the risks of the complications mentioned above, "has no special importance". The admission to hospital of all serious cases of streptococcal pharyngitis is strongly recommended, and to make room for them mild and uncomplicated cases of scarlet fever should be discharged.

C. McNeil

1812. **Prevention of Epidemic Neonatal Diarrhoea**

D. M. STERN. *Lancet* [*Lancet*] **1**, 80–81, Jan. 11, 1947.

Neonatal diarrhoea is defined as a disease of infants in the first three months of life; it is characterized by frequent loose stools, at first green, then yellow or orange, but sometimes formed and passed from the bowel with accompanying liquid which soaks into the napkin and may be mistaken for urine. Resultant dehydration leads to progressive loss of weight; the younger the infant the shorter is the incubation period, and the more severe the disease. Premature, weakly, deformed, and dyspeptic infants especially are attacked. Vomiting is a feature of some cases. The disease may occur sporadically or in epidemics, and is not to be confused with endemic gastro-enteritis, which attacks adults as often as children. This latter disease is probably an air-borne virus infection, and is usually non-fatal.

The author's views on prevention are based on wartime experience of three epidemics occurring at two hospitals. The first epidemic, at West Middlesex County Hospital, began in a small ward of premature infants, whence, despite every effort and ingenuity in prevention and treatment, it spread during 9 months throughout the maternity unit; 53 out of the 68 babies attacked died. The only common factor in all cases was the use of pooled feeding bottles and teats. The second epidemic, at Chiswick Hospital, was checked after only two cases, apparently by withdrawing all bottles and spoon-feeding all babies needing artificial feeds, whether supplementary to, or in substitution of, breast feeding. The milk mixture was not changed, only the method of offering it to the babies. The third epidemic, which was less virulent than the other two, was again at the West Middlesex County Hospital and 7 out of the first 9 patients died, the remaining 23 recovering after the substitution of spoon-feeding for bottle-feeding.

An attempt is made to rationalize the observations that: (1) bacteriological investigations revealed that bottles used for infant feeding gradually acquire on the inside an ever-thickening deposit of protein and fat which makes them resistant to sterilization and promotes the growth of other organisms introduced into them; (2) the breast-fed baby never gets the disease, or only when given supplementary bottle feeds; (3) the bottle-fed baby in a hospital or nursing home gets it more often than the bottle-fed baby at home, and in the institution where feeding bottles are pooled the baby gets it more often than the baby which has the same bottle throughout its stay; (4) an affected baby improves on water alone, but relapses when it returns to milk; (5) different organisms are found in different epidemics, some sulphonamide-resistant and some not; (6) substitution of spoon-feeding for pooled feeding bottles and teats checked two epidemics. It is suggested that the baby fed from the one bottle at home or in hospital can get "acclimatized" even to the non-sterilizable bacteriological film—that is, its resistance grows with the film—whereas the baby fed from pooled bottles may be suddenly subjected to a massive dose from a heavily-infected film. [Another explanation could be that the change of bottle re-infects the infant with a new strain of organism or virus. There is the common experience at fever hospitals that the secondary streptococcal strain infection may be a good deal more severe than the primary.] The author recommends that: (1) further attempts should be made to identify causal organisms by bacteriological examination of feeding bottles during epidemics; (2) separate bottles and teats should be used for every baby, or, if pooled bottles must be used, the bacteriological film should be cleaned off before the bottle is sterilized; (3) teats should be replaced frequently, the old ones being destroyed.

J. Greenwood Wilson

1813. **Immunization in Children**
J. H. B. GRANT. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **55**, 493–497, Nov., 1946. 4 refs.

1814. **Pink Disease: A Review of 65 Cases**
T. N. FISHER. *British Medical Journal* [*Brit. med. J.*] **1**, 251–253, Feb. 15, 1947.

The 65 cases described were seen over a period of 14 years, and 62 were followed up; 53 patients recovered completely and 9 died (14·5%). The cause of death in 6 was secondary infection, 1 died suddenly in hospital, and in 2 the cause could not be ascertained. Pink disease shows no seasonal incidence; the highest age incidence is between 5 and 12 months. Neither social nor financial status has any aetiological significance, nor is there any evidence that the disease is due to vitamin deficiency. The average duration of the illness in 46 children who recovered was 4 months. Characteristically the onset is insidious and not preceded by dietetic disturbance or ill-health. There are three basic symptoms: a profound change in temperament, muscular hypotonia, and tachycardia. Other features of the disease, such as the rash, perspiration, and affections of the eyes and mouth, vary considerably in their onset, intensity, and duration. These infants are very susceptible to secondary infection of the skin and of the respiratory tract, and are best nursed in their own homes. Treatment has been symptomatic, the cause of the disease being unknown. The guiding principles in management are scrupulous attention to bodily hygiene, infinite patience in feeding, and the use of sedatives and local soothing applications.

Jas. M. Smellie

1815. **Parenteral Administration of Ammonium Chloride for Alkalosis of Congenital Hypertrophic Pyloric Stenosis. A Preliminary Report**
G. B. FORBES and J. A. ERGANIAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **72**, 649–660, Dec., 1946. 7 figs., 13 refs.

The pre-operative preparation of infants with congenital pyloric stenosis plays an important part in the ultimate prognosis, establishment of normal fluid and of acid-base equilibria being two of the chief aims. The tendency to alkalosis as a result of the continued vomiting can usually be satisfactorily counteracted by dextrose and Ringer's solution given parenterally. Adequate renal function, however, is essential for this, and if it is impaired by persistent anhydraemia or pre-existing renal disease the alkalosis will be unaffected.

Reference is made to 3 infants whose alkalosis was so severe that they died before operation could be undertaken and to 2 more who nearly died after operation because their acid-base equilibrium had not been adjusted. As a result of these setbacks the authors decided to study the effect of ammonium chloride given parenterally in such cases. The ammonium radical is converted into urea by the liver, and the chloride is released to combine with the fixed base in the body fluids. Because the vomitus in cases of pyloric obstruction contains appreciable amounts of sodium in addition to chlorides it was decided to add normal saline or Ringer's solution to the ammonium chloride in sufficient quantity to make a one-sixth molar solution of the ammonium salt (8·9 g. ammonium chloride per litre). This gives a *p*H of 5·2.

The solution is sterilized by autoclaving and remains stable for several months.

After animal experiments clinical trials were made, and the authors describe 9 cases in infants with congenital pyloric stenosis who showed significant elevation of serum bicarbonate. It was found that the change in serum bicarbonate, *p*H and chloride was prompt, appreciable changes occurring within a matter of minutes. Transient rises of non-protein nitrogen in the serum were observed but were not significant. Dosage was from 30 to 60 ml. per kilo body weight, either subcutaneously or intravenously, but no constant relationship was found between the amount of ammonium chloride given and the resultant drop in serum bicarbonate. The authors stress that the other important pre-operative details should not be overlooked and that treatment with ammonium chloride should be limited to those infants for whom accurate chemical data are available.

[In view of the generally good response of infants with congenital pyloric stenosis to the usual pre-operative routine with plasma or saline-glucose and the relative infrequency of manifest alkalosis or pre-existing renal disease in these cases, this work would seem to be of limited application.] *W. F. Gaisford*

1816. **Lymphosarcoma in Children.** (Il linfosarcoma nel bambino)
M. Bolletti. *Pediatria del Medico Pratico* [*Pediat. Med. prat.*] **19–21**, 427–454, Oct., 1946. 2 figs., 60 refs.

This paper details the conclusions reached by the author after a study in the literature of some 70 cases of lymphosarcoma occurring in infancy and childhood. The investigation was prompted by the occurrence within a very short period of 3 cases of lymphosarcoma in children at the university paediatric clinic of Padua, no case having been seen there for the previous 13 years. All the case-histories examined, including the 3 reported in this article, were of children under the age of 10.

Lymphosarcoma is comparatively rare among children, compared with its incidence in adults, and boys are twice as commonly affected as girls. Though the disease may occur at any age in childhood, it seems most common between 4 and 7 years. Several cases have been reported very early in life, and a few, affecting chiefly the liver, were probably intra-uterine in onset. The primary site of origin, in so far as it could be accurately ascertained, is most frequently in the mediastinum, from thymus or tracheo-bronchial lymph nodes; less common sites are the lymph follicles of the alimentary canal and the retroperitoneal and mesenteric glands. Primary onset in the lymphatic tissue of the pharynx or in the lymph nodes of the neck, the most frequent site in adults, is very rare in children. Metastasis is not by the blood stream but occurs by permeation of lymphatics, with displacement and compression of tissues but not destruction. Spread may occur to any part of the body, but the spleen and bone marrow are characteristically very rarely affected. The spleen was infiltrated in only 4 out of 70 cases, and even in these it was not clinically enlarged. With the primary site in the chest, invasion of lungs, heart, and pleura may occur often with transdiaphragmatic spread to retroperitoneal and other abdominal nodes. The liver is not often affected, but much more so than the spleen, hence the absence of splenic enlargement is frequently of considerable diagnostic importance.

Lymphosarcoma runs a more rapid course in the child than in the adult, and in the majority of cases the time elapsing between onset of symptoms and death is not more than 2 to 3 months. The disease is usually accompanied by irregular fever, which in the adult is merely a terminal event. Symptoms vary according to site, but the most common are a persistent dry cough, dyspnoea, pleural effusion, abdominal distension, and vague pains in the abdomen. Intestinal obstruction is rare. Sudden death may occur before obvious signs or symptoms have had time to manifest themselves, from involvement of a vital organ such as the heart. Lymphocytopenia, to which some authors attach importance in diagnosis, is rare in cases in childhood, and is shown only with widespread disease. No periods of remission, however brief, are seen in children. *X* rays and radium are useless, and arsenic and lead used in the highest possible doses, though they may cause a temporary amelioration, have no real effect on the course. No cases have been reported of recovery in childhood, even after radical surgical intervention in early cases. There are no known aetiological factors or predisposing causes.

In the differential diagnosis of lymphosarcoma the sarcomata and carcinomata of childhood have to be considered, together with Hodgkin's disease, syphilitic and tuberculous granulomata, the acute leukaemias, and especially mixed tumours of the kidneys. The author considers that there should be little difficulty in diagnosis if the study of the clinical picture is associated with biopsy, which shows a delicate reticulum, in the meshes of which lie cells of a lymphoid character which are not as small or as darkly staining as true lymphocytes. Biopsy, in the frequent absence of peripheral metastases, should be carried out by exploratory needling—a procedure which in the author's experience rarely presents difficulties. Full case-histories are given of 3 boys with abdominal lymphosarcoma, probably originating respectively in retroperitoneal and omental lymph nodes and gut. *E. G. Sita-Lumsden*

1817. **Gallop Rhythm in Children, studied by means of Calibrated Phonocardiography. An Experimental and Clinical Investigation.** [In English]
L. E. Carlgren. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **33**, Suppl. 6, 1–141, 1946. 20 figs., 128 refs.

1818. **Mentally Deficient Children of Various Types and Ages and Their Expectation of Life.** (Über das Vorkommen von schwachsinnigen Kindern verschiedener Typen und verschiedenen Alters sowie über ihre Möglichkeiten am Leben zu bleiben)
N. Hallman. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **33**, 287–320, Dec. 30, 1946. 1 fig., 23 refs.

1818*a*. **Dacryostenosis**
H. W. Price. *The Journal of Pediatrics* [*J. Pediat.*] **30**, 302–305, March, 1947. 3 refs.

Medicine: General

1819. **A Study of the Structural and Hormonal Reactions of the Pituitary Body of Rats Exposed to Cold.** [In English]
S. E. BROLIN. *Acta Anatomica* [*Acta anat.*] Suppl. 3, 1–169, 1946. 34 figs., 232 refs.

The thyroid of animals exposed to cold increases in size, and histological evidence shows that functional stimulation occurs. The mechanism of this hyperthyroidism has not hitherto been known with certainty. The adrenal cortex also plays a fundamental part in the reaction of the body to cold. In the absence of the adrenals the necessary increase in the production of heat does not occur. There is good evidence that the adrenals not only adapt themselves to the changed conditions but also take an active part in the chemical regulation of body temperature. Whether the cortex is stimulated directly by the anterior pituitary or by the thyroid was not hitherto known. The anterior pituitary is necessary for the functional activity of both thyroid and adrenals, but it need not follow from this that it is the primary activator in cold conditions. Previous investigations into this question have been made under such severe conditions as to cause structural damage. Those described in this paper had as their object the determination of the relative parts played by the three glands in the normal reactions of the animal body to cold not severe enough to cause structural damage. The rat was chosen as the experimental animal because its anterior pituitary had been shown to have a high thyrotrophic activity—in comparison with the guinea-pig, whose pituitary appears to secrete little thyrotrophin. The pituitary of the rat manifests more clearly than that of other animals the changes induced therein by thyroidectomy and may therefore be expected to show most clearly the effects of any other stimulus to increased thyrotrophic activity. Moreover, it has previously been shown that anti-hormones are not formed in the rat in response to injections of its own pituitary hormones. Day-old chicks were used as test objects for the demonstration of thyrotrophic hormone.

Male and female rats were kept for several weeks at two different ranges of temperature: (1) between +5° and +10° C., and (2) between +1·5° and +3° C. At both temperature levels their health was unimpaired. Statistical analysis showed that the pituitary suffers a significant loss in total weight after exposure to cold, due to a decrease in size of the partes anterior and intermedia; the weight of the pars posterior is unchanged. On the other hand, there is an increase in weight of the adrenals at the higher range though not apparently at the lower. The testicles show no change in weight, though the seminal vesicles and prostate are reduced in size. Histologically the gonads, vaginal epithelium, adrenals, and intermediate and posterior pituitary lobes are unchanged. The thyroid shows signs of increased activity. In the anterior pituitary enlargement and vacuolation of the basophil cells occur. These changes, though quantitatively less, are qualitatively identical with those seen after thyroidectomy, and it may therefore be that they are the expression of increased activity. In order to test this hypothesis, the serum and urine of control animals and those exposed to cold were tested for thyrotrophic activity, the criterion being the effects of extracts on the height of the acinar epithelium of the thyroids of day-old chicks. Thyrotrophic hormone was demonstrated in the serum and urine of the rats exposed to cold but not in the controls. It may therefore be assumed that the relative hyperthyroidism which occurs in response to cold is due to an increased secretion of thyrotrophic hormone by the anterior pituitary and that the changes seen in the basophil cells are in fact an expression of increased activity. [This observation may be regarded as further evidence that vacuolation of the basophils in other conditions, such as Cushing's syndrome, is a sign of increased activity.] This vacuolation may be prevented in thyroidectomized rats at normal temperatures by the injection of thyroxine. The injection of thyroxine into thyroidectomized rats exposed to cold likewise prevented changes in the basophil cells. On the other hand, the increase in weight of the adrenals which occurs in rats exposed to cold was not prevented by thyroxine. It follows that the reaction of the adrenals to cold is independent of the secretion both of thyroxine and of thyrotrophic hormone.

Bilateral cervical sympathectomy was performed on certain of the rats. In the pituitaries of sympathectomized rats the basophil reactions are more pronounced in the animals exposed to cold than in those kept at normal temperatures, and not less, as might be expected. The activity of the anterior pituitary is therefore not dependent in this respect on its sympathetic innervation. On the other hand, the heat regulation of rats whose pituitary stalk has been cut is defective, and many of the rats exposed to cold die. In female rats cutting the stalk results in a variable degree of hypogonadism, and in males degenerative changes occur in the germinal epithelium and there is a reduction in weight of the testicles, seminal vesicles, and prostate. These changes occur irrespective of temperature, which appears to have no influence on gonadotrophic function in rats with cut stalks. Thyrotrophic function is definitely reduced also by cutting the pituitary stalk, and no increase in thyrotrophic activity can be induced by cold in rats so treated. The basophil changes previously referred to do not occur. The cells appear to be unable to respond to cold when their connexion with the hypothalamus has been severed. Nevertheless it is still uncertain whether thyroxine depresses the pituitary directly or indirectly by way of the hypothalamus.

In view of the multiple effects of the secretion of the basophil cells, the question arises as to whether the

increase due to cold in their thyrotrophic activity is reflected in their own functions, such as gonadotrophic activity. These experiments show that in cold the activity of the basophil cells increases. On the other hand, the weight of the anterior pituitary decreases. There is probably an increase not only in activity but also in the consumption of cells, similar to that which has been found in response to an increased call for gonadotrophin. In the latter circumstances it has been found that when there is an increase in stored gonadotrophin (as in the castrate) there is a diminution in stored thyrotrophin. Conversely, after thyroidectomy, when there is an increase in stored thyrotrophin there is a decrease in stored gonadotrophin. After exposure to cold the testicles are undamaged but, judging from the decreased size of seminal vesicles and prostate, somewhat inactive. This is presumably due to a decrease in gonadotrophic secretion, corresponding to an increase in thyrotrophic secretion.

[On the hypothesis that the secretion of the basophil cells is unitary and that the thyroid and the gonads each make use of the appropriate prosthetic group an increase in thyrotrophic activity might be expected to carry with it an increase in gonadotrophic activity. On the other hand, if the basophils are capable of producing either thyrotrophic or gonadotrophic hormones alone, an increase in the production of one might result in a decrease in the production of the other, the one with the highest momentary survival value having priority. This very important monograph should be read in the original. The conclusions reached are of a clinical importance far beyond the question of mere adaptation to cold.]

Raymond Greene

ALLERGY

1820. **Studies on Ragweed Pollen Sensitization in Rabbits and Guinea Pigs.**

A. M. KULKA and D. HIRSCH. *Journal of Immunology* [*J. Immunol.*] **53**, 391–399, Aug., 1946. 16 refs.

This study is a continuation of earlier work on sensitization to ragweed pollen and the production of antibodies by means of adjuvants in rabbits under observation for 2 years. The second part deals with the nature of passively sensitizing antibodies in guinea-pigs against ragweed pollen extract. The antigen–adjuvant mixture was prepared as follows: 8 ml. of ragweed pollen extract in 10 ml. of salt solution was added gradually to 10 ml. of " aquaphor " (a lanolin-like preparation) in a mortar and blended thoroughly; 20 ml. of heavy paraffin oil containing 4 mg. of killed tubercle bacilli was mixed in the mortar with the combination of pollen extract and aquaphor. All this was done with aseptic precautions and the mixture was kept in sterile rubber-capped vials. Rabbits treated with ragweed pollen extracts with or without adjuvant for a year were treated for a second year and the collodion agglutinating titre of the serum, cutaneous sensitivity, and passively sensitizing antibody content were tested from time to time. The pollen extract used before contained 2,000 protein nitrogen units (p.n.) per ml., and single injections consisted of 500 to 10,000 units. In this study the p.n. concentration was 10,000 units, allowing 20,000 to 100,000 p.n. units per dose. To avoid severe local reaction the adjuvant should not exceed 0·5 ml. Rise of agglutination titre was observed (up to 1 : 320) in sera with previously low titre (1 : 40), but no rise in the case of those with previously high agglutination titre. A fall (negative phase) and subsequent rise was observed after the injections. Skin sensitivity had a tendency to decrease with time. Successful passive sensitization does not necessarily coincide with a high agglutination titre.

The agglutination titre was in direct relation to the number of injections, the highest titre observed being 1 : 1,280 in guinea-pigs. They were injected with alum-precipitated ragweed pollen extract. The animals' serum was used for passive sensitization of guinea-pig and human skin. The sera from the blood samples were preserved with 1 : 10,000 " merthiolate " and stored in sterile rubber-capped vials. Skin sensitivity to ragweed pollen extract was tested in the guinea-pigs 2 weeks after the last injection. Four months after the first injection the serum was taken, preserved, and used to inject a shock dose intracardially or intravenously. Two sets of 27 and 20 animals were used in these experiments.

From another group of 24 guinea-pigs, treated with ragweed extract and adjuvants, 21 transferred sensitizing antibodies to normal guinea-pig skin. There was no relation between the agglutination titre and their ability to transfer passive sensitization. Sixteen sera produced passive sensitization of the human skin. A 1 : 10 dilution of the serum was used, since this transfers passive sensitization as well as undiluted serum but without causing toxic necrosis of the skin. Even guinea-pig serum diluted 1 : 100 sometimes transferred passive sensitization. There was no correlation between the concentration of the passively sensitizing antibodies present in the serum and the severity of the anaphylactic shock in the animals tested or their skin sensitivity.

E. M. Fraenkel

1821. **Chromidrosis Associated with Ragweed Hyposensitization**

H. C. HAYDEN. *Annals of Allergy* [*Ann. Allergy*] **4**, 372–373 and 387, Sept.–Oct., 1946. 3 refs.

Chromidrosis is a rare disorder of unknown origin with excretion of coloured sweat. This may be tinged yellow, red, green, blue, or black when excreted, or develop the colour by oxidation in the air or when uniting with substances on the surface of the skin. Most common are cyanidrosis (blue) or melanidrosis (black), which are due to indigo, an oxidized derivative of indoxyl, that originates in the intestinal tract. Other colours may be due to ingestion, or absorption by contact, of substances such as potassium iodide, copper, or iron, or, as in the case of reddish axillary sweats, to chromatogenic bacteria (pseudochromidrosis). A woman of 58 who had suffered from pollinosis (grass and ragweed) for 46 years noticed discoloration of her face-cloth every year for 8 to 9 years about Aug. 15; this lasted through the season, and disappeared with the onset of

cold weather. Dust, grass, and ragweed desensitization in the tolerated doses had been given. In 1945 the discoloration began about June 10—6 weeks after the start of the course of ragweed desensitization—and disappeared for 14 days while this was interrupted. The bluish tinting continued mildly during the summer, and became accentuated late in August and in the first two weeks of September. It disappeared, as usual, with the advent of frosty weather. A blue substance was extracted from the face-cloths that behaved chemically like indigo. *E. M. Fraenkel*

1822. **The Integration and Differentiation of Allergic Phenomena**
R. R. DOERR. *Annals of Allergy* [*Ann. Allergy*] **4**, 339–351, Sept.–Oct., 1946. 72 refs.

Allergic reactions are caused by specific substances, and the allergic patient does not react more strongly than the normal individual, but in a different manner. In the study of anaphylactic reactions a good explanation is found for allergic phenomena, and their separation from these is not justified. A precipitation of surplus antigen *in vivo* as a cause of the anaphylactic reaction and the reaction of antibody with antigen in solution in cases of passive anaphylaxis can be assumed. The relation between the antigen-antibody reaction and the release of histamine is not yet clear. It has been observed in the rabbit, the calf, and the horse that in anaphylactic shock the histamine content of the blood is not increased but decreased. There are other species differences—for example, in the Schultze-Dale test, which is negative in rhesus monkeys. Allergy is therefore not simply a special type of anaphylaxis. The long persistence of anaphylaxis in sensitized guinea-pigs over more than a year suggests that the antibody production may become independent of the stimulus of the antigen, once it has been started. *E. M. Fraenkel*

1823. **Allergic Causes of Pruritus Ani**
F. R. RUGELEY. *Annals of Allergy* [*Ann. Allergy*] **4**, 374–378 and 396, Sept.–Oct., 1946. 6 refs.

The association of pruritus ani with allergy is rarely acknowledged. It is, however, necessary to consider carefully the aetiology of these conditions in order to improve therapeutic results. The objective findings, such as excoriation, oedema, thickening of the skin, and exudation, vary in degree and intensity, and cryptitis, papillitis, alterations in *p*H, and fissures are often secondary and not primary changes. In 14 cases, previously treated unsuccessfully by other methods, a careful aetiological study was made. Apart from a careful history, an allergic survey of contact or ingested allergens by skin tests, elimination diet, local examination and examination of the blood for eosinophils was carried out in addition to proctoscopic and prostatic investigation. Patch tests suggested contact allergy in some of the cases; skin tests, elimination diet, or the presence of other allergic signs revealed allergic causes in others, and treatment on these lines brought rapid improvement. Allergic causes of pruritus ani should therefore be investigated before radical procedures are suggested, such as surgery, *x*-ray treatment, injections, division of nerves, or tattooing of the anal margins with anaesthetics. *E. M. Fraenkel*

1824. **Contact Dermatitis from Japanese Rifles**
F. HINMAN. *Annals of Allergy* [*Ann. Allergy*] **4**, 384–387, Sept.–Oct., 1946. 3 figs., 3 refs.

Japanese rifles were distributed to the crew of an American aircraft carrier, and 150 ratings removed the varnish from the stocks, using scrapers and sandpaper without wearing gloves. Their hands were merely washed with soap and water, and 7 of the men subsequently developed skin lesions severe enough to lead them to report sick; 2 had to be admitted to the sick-bay. Dermatitis occurred in over 4·5% of those exposed, and was probably due to the varnish on the rifles. It is suggested that this may have been made from the sap of *Rhus vernicifera*, a species of sumac, generally used as common natural varnish in Japan. This is related to the toxic (allergenic) *Rhus toxicodendron*. A vesicular dermatitis developed on hands, forearms, and other exposed parts 2 days after exposure to " sanded " varnish of captured Japanese rifles in individuals who were found to be allergic to plants (poison ivy) or other allergens. The single exposure and the ready response to removal of the allergen and to mild local treatment incriminate the varnish as the cause of the contact dermatitis. As controls 7 (probably not sensitive) men who worked in the ship's armoury and had also been cleaning and handling these rifles were interviewed; none of them had noticed itching or eruptions; neither had members of the hospital staff, with a negative personal or family history of allergy, who were observed while " refinishing " rifles. *E. M. Fraenkel*

1825. **The Treatment of Penicillin Urticaria with Nicotinic Acid**
W. C. SERVICE. *Annals of Allergy* [*Ann. Allergy*] **4**, 397–398, Sept.–Oct., 1946. 1 ref.

The author observed 41 cases of allergic reactions to penicillin and successfully treated them with intravenous injections of nicotinic acid. Urticaria was most common and was seen in 37 cases, in 15 of them as a diffuse papular eruption all over the body. In the other 22 patients massive areas of whealing developed, with the itching chiefly confined to the edge of the wheal. Twelve had angioneurotic oedema of the face, especially of the orbital areas, and in 2 it affected the genitalia. In 3 of the more severe cases of urticaria signs of typical serum disease developed, with swelling and stiffness of the joints, raised temperature, and albumin in the urine. After the application of penicillin to the eyes 3 cases of contact dermatitis occurred, and there was 1 case of eczematoid dermatitis of the leg at the site of a varicose ulcer, where penicillin had been employed in an ointment base. Treatment with the usual drugs, such as adrenaline, ephedrine, calcium gluconate, vitamin K, morphine, and " benadryl ", gave only transient relief. The author

claims that intravenous injection of 35 mg. of nicotinic acid in 8 to 10 ml. of distilled water was successful in these 41 cases. The injection should be done very slowly, and should be stopped when the patient feels a sensation of flushing after 3 to 4 ml. has been given; the needle is kept in place and the injection resumed after a few minutes when the sensation subsides. No further signs of a flush occurred, and permanent relief was obtained after a few hours, except in 4 cases, where a second injection had to be given the next day and proved successful. *E. M. Fraenkel*

1826. **Use of "Benadryl" for Penicillin Urticaria. Preliminary Report**
R. R. WILLCOX. *British Medical Journal* [*Brit. med. J.*] **2**, 732–733, Nov. 16, 1946.

Penicillin urticaria often manifests itself at the end of a 7½- or 12-day course in the treatment of syphilis. Reports of 6 cases of urticaria—5 following intramuscular penicillin and 1 following sulphonamides (Case VI)—are presented. In Cases I and IV, on "benadryl" 50 mg. thrice daily for 24 hours, the urticaria cleared in a day. In Case II 350 mg. of benadryl was given over 2¼ days and the urticaria completely disappeared in 3 days, the usual duration before improvement being about 4 days. Case III was given adrenaline min. 10 (0·6 ml.) twice and ephedrine gr. ½ (32 mg.) thrice on the first day. On the following day the urticaria was unchanged, and benadryl 50 mg. thrice daily was given. On the third day, after a total of 200 mg. of benadryl, the rash was worse and 10 minims of adrenaline was given. This resulted in a severe collapse, followed by a pyrexia of 101° F. (38·3° C.). It was thought that the collapse might in some way be related to the concurrent administration of benadryl. No further benadryl or adrenaline was given. In Case V severe generalized urticaria, oedema, and joint effusions cleared after benadryl 50 mg. thrice daily for 3 days. On the following day a relapse occurred, which was treated with ephedrine and took 5 days to subside. In Case VI the urticaria was accompanied by bullae on the hands and occurred after sulphonamide therapy. Benadryl 50 mg. thrice daily for 3 days had no effect on the bullae but caused disappearance of the urticarial patches in 24 hours. Five days later a relapse occurred, responding in 48 hours to benadryl 50 mg. thrice daily given for 3 days. *D. A. Williams*

1827. **Allergic Reactions to Penicillin**
A. I. SUCHECKI. *British Medical Journal* [*Brit. med. J.*] **2**, 938–940, Dec. 21, 1946. 11 refs.

The author has collected 38 cases from the literature and has added 9 of his own with allergic reactions to the administration of penicillin parenterally and locally. Reactions have been classified into 4 groups: (1) Effusion into a large joint occurring 2 to 5 days after starting treatment and subsiding in 8 to 10 days. (2) Urticaria becoming manifest any time during the treatment. (3) Reactions simulating serum sickness, including bronchospasm, arthralgia, skin involvement, and a severe general reaction occurring during treatment or several days after its termination. (4) A syndrome resembling anaphylactic shock. Subcutaneous injections of adrenaline hydrochloride generally give rapid relief. Skin tests give variable results, and the author suggests that a preliminary injection of 15,000 units might produce a clear-cut and mild enough reaction to indicate a penicillin reactor. It is not yet certain whether the sensitivity results from the penicillin or one of the impurities contained in the preparation. *Noah Morris*

1828. **Generalized Angioneurotic Edema due to Penicillin Inhalations Treated with Benadryl**
D. SCHEINBERG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 78–89, Sept. 14, 1946.

Ten days after starting penicillin inhalations—25,000 units 4 times a day—a man of 54 developed severe generalized angioneurotic oedema. "Benadryl", 4 capsules (50 mg. each) on the first day, reduced the swelling and the pruritus, and another 10 capsules during the next 24 hours resulted in complete recovery. While on benadryl he felt "dopey", but this disappeared when it was stopped. *D. A. Williams*

1829. **Bronchial Asthma in the Young Male Adult. A Study of Fifty Patients Returned from the Tropics for Bronchial Asthma, as Compared to Fifty Asthmatics Stationed in the United States**
F. L. ROSEN. *Annals of Allergy* [*Ann. Allergy*] **4**, 391–396, Sept.–Oct., 1946. 21 refs.

Asthma has been a common cause of medical casualties in the American Forces serving in the tropics, and 50 patients recently returned from that region because of bronchial asthma are compared with 50 asthmatics stationed in the U.S.A. Of those returned from the tropics 40% had their first attack while in that area, compared with 14% in the U.S.A. who had had their first attack after enlistment: 20 patients compared with 7—nearly 3 times the incidence in the U.S.A. Eosinophilia of 5% or more occurred in 42% of the tropical group and in 32% of the U.S.A. group. In a tropical control group of 50 patients with malaria or non-allergic respiratory disease only 2 (4%) had an average eosinophilia of 5% or more. In all the asthma patients examination proved the absence of parasites or ova. *X*-ray findings in the chest were normal in 84% of the tropical group and in 82% of the home group, and no relation was found between *x*-ray findings and hypereosinophilia. Timothy grass pollen gave more frequent positive skin tests (42% compared with 26% in the U.S.A.), and feathers gave less frequent reactions (6% compared with 24%). Tests with moulds (*Alternaria* and *Hormodendron*) yielded unexpectedly few positive reactions (7% compared with 5% in the U.S.A.). As a possible cause of the greater frequency of asthma in American soldiers in the South-West Pacific (bronchial asthma, or "guha", is endemic in Guam and the Micronesian Islands) inhalants such as coral and copra dust, rice and cane-sugar pollen, as well as grass pollen, have been

suggested. Intense sunlight and the scents of flowers and fruits may also be factors. *E. M. Fraenkel*

METABOLIC DISORDERS

1830. **Protein Deficiency—a Nutrition Problem.** (Eiweissmangel als Ernährungsproblem)
J. KÜHNAU. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **1**, 161–166, Sept. 30, 1946. 42 refs.

This article is based on the literature of proteins and amino-acids and on recent clinical and biochemical observations made in Germany by the author and others. In that country now there is an absolute deficiency of protein and the quality also is poor. This is due partly to energy deficiency, because much of the dietary protein has to be diverted to supply energy. Evidence of undernutrition mainly takes the form of protein deficiency, but the effects of lack of essential fatty acids, of minerals, and of vitamins are also seen. Oedema is the commonest symptom; its immediate cause is lowering of the blood proteins, particularly albumin, which is mainly responsible for the osmotic pressure of the proteins. Citing Whipple and others, the author asserts that blood proteins can be re-formed with speed and certainty only by consumption of animal protein; soya and perhaps potato protein come closest to animal protein in this respect. To replace the daily loss of 6 to 10 g. of blood protein, the administration of 15 to 20 g. of blood protein, 36 to 60 g. of muscle protein, 60 to 100 g. of casein, or much more potato protein is necessary; all other plant proteins by themselves would not suffice. The author estimates the daily requirement of the 10 essential amino-acids to be 36 g. for adolescents and 22 g. for adults (requirements of individual amino-acids are tabulated). The British Zone rations in 1946 gave totals of 11 and 9 g. of the essential amino-acids, compared with estimates made in 1937 of 53 and 31 g. for adolescents and adults respectively.

The author argues that protein deficiency leads to disturbances of digestion, absorption, and endocrines and to polyneuritis, although the low blood proteins in liver cirrhosis are not influenced by the amount and quality of protein in the food. Protein-rich food protects the liver against infections and toxins, and protein-poor food predisposes to liver disease; methionine is of particular significance in these respects. The essential amino-acids play a dual role—in construction and repair, and for special metabolic purposes after the fashion of the vitamins. The present rations are especially poor in lysine, phenylalanine, and methionine; the adolescent's ration provides only 17% of his requirements of lysine. In oedema, of the amino-acids cystine and methionine are much reduced, tyrosine but slightly, and tryptophan not at all. The health of the next, as well as of the present, generation will be damaged if more and better protein is not soon made available. In the absence of supplies of animal proteins, soya flour should be provided, also more bread, which should contain some barley and oats to raise its protein value. *H. E. Magee*

1831. **Haematological Changes in Certain Syndromes due to Dietary Deficiency ("Burning Feet" and Retrobulbar Neuritis).** (Enkele mededeelingen omtrent afwijkingen in het bloedbeeld bij patiënten met neuritis retrobulbaris en "Burning Feet" als voornaamste voedingsdeficiëntie-verschijnsel)
J. F. DE WIJN. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **90**, 1439–1445, Oct. 19, 1946. 4 figs.

The results of a haematological study among prisoners of war in Java and Japan are presented in four tables. The first shows the blood picture of 8 apparently healthy men who had other sources of food in addition to their camp diet. This picture is normal. The second table illustrates 5 still healthy cases, but the count was made 6 months later, when the food situation became worse and the supply of additional food from outside stopped. A leucopenia of 4,300 to 4,900 cells per c.mm. is now seen and a tendency to a toxic granulation of the neutrophil leucocytes. The third table (27 cases) and the fourth (8 cases) show the blood picture of men presenting pathological symptoms, such as "burning feet" and "camp eyes". In these cases the number of leucocytes was either normal or slightly diminished; there was a neutropenia with a relative lymphocytosis in 66 to 75% of the cases; toxic granulations appeared in 60% of the mild and in 80% of the serious cases. A remarkably high proportion of the cases (47%) had eosinophilia, although no parasites were detected. The number of erythrocytes and the percentage of haemoglobin kept near the lower normal limit, but the red-cell diameter was increased (7·9 to 8·7 μ). This macrocytosis, though not found among the apparently healthy prisoners, was present in those suffering from both beriberi and pellagra and was particularly conspicuous in cases with chronic alimentary affections.

Diagrams of the Price-Jones curve illustrate further the modifications in size of the erythrocytes. Thus in 2 cases of retrobulbar neuritis with "burning feet"—1 of them of 3 months' and the other (a relapse) of 10 months' duration—the curve had shifted considerably to the right and its top was flattened. In another case of pellagra, submitted for 3 weeks to an intensive course of liver therapy, the shift to the right was still there but a second top appeared along the dividing line of normal average values. The cellular diameter was determined by a modification of the Price-Jones method, made necessary by the lack of proper equipment. This method was later satisfactorily tested for correctness. It was found that the blood changes occur as soon as the clinical symptoms begin, and that they disappear with the latter, to become evident again during a relapse. The macrocytosis thus acquires diagnostic importance. Another constant sign in the cases described was hypoacidity of the gastric juice and sometimes even achylia.

The author concludes that the toxic-degenerative changes in the white cells were due to vitamin-B deficiency, which inhibited the mature development of the myeloid cells. The eosinophilia found in 47% of the cases points to the existence of an allergic state, and a liability to skin diseases seems to confirm this hypothesis. The

macrocytosis cannot be entirely ascribed to the lack of the extrinsic factor, as this would have ultimately produced pernicious anaemia. It is more probable that the increased size of the red cells was due to the impairment of liver function brought about by the disturbance of the food metabolism resulting from the multiple deficiency. *A. Lilker*

1832. **Alterations of Neuromuscular Excitability in Alimentary Imbalance and the Avitaminoses. XIV. The Part Played by the Principal Vitamins in Maintaining the Acid–Base Equilibrium of the Organism.** (Les troubles de l'excitabilité neuromusculaire au cours des déséquilibres alimentaires et des avitaminoses. XIV. Rôle des principales vitamines dans le maintien de l'équilibre acide–base de l'organisme)
R. Lecoq, P. Chauchard, and H. Mazoué. *Bulletin de la Société de Chimie Biologique* [*Bull. Soc. Chim. biol.*] **28**, 595–600, July–Sept., 1946. 16 refs.

It has previously been shown that lack of vitamin A or E or of the vitamin-B complex changes the chronaxia of nerves and muscles in the same way as a condition of acidosis, and lack of vitamin C or D in the same direction as a condition of alkalosis. The effects of these vitamins on the chronaxia of the extensor and flexor muscles of the toes and of their motor nerves are now studied in normally fed rats in which a state of acidosis has been induced by the daily or thrice-weekly subcutaneous or intraperitoneal injection of 25 mg. of ammonium chloride, or a state of alkalosis by the similar injection of 12·5 mg. of sodium bicarbonate. Vitamin A (12·5 μg.) injected daily in oil, or 5 μg. of aneurin, 5 μg. of riboflavin, 100 μg. of nicotinamide, and 150 μg. of adenine injected together in water, or 2·5 mg. of α-tocopherol injected in oil, kept the chronaxia normal in the cases of acidosis but had no effect in cases of alkalosis. On the other hand, 20 μg. of calciferol in oil or 5 mg. of sodium ascorbate in water corrected the neuromuscular changes of alkalosis but not those of acidosis. The individual components of the B complex alone or administered in combinations of two or three were without action, as was the addition of 100 μg. of pantothenic acid.

Daily injections of 1·5 mg. of vitamin A diminish the nerve chronaxia in normal rats, while 2·5 mg. of vitamin E or 12·5 μg. of carotene prolong it, the muscle chronaxia being changed in the opposite sense in each case; but, while both vitamins A and E oppose the effects of acidosis and augment those of alkalosis, carotene is without action on the neuromuscular effects of disturbed acid–base balance, and so cannot replace vitamin A in this respect. None of the effects described are obtained by the administration of the vitamins by mouth.
T. R. Parsons

1833. **Hunger Oedema.** (Über das Hungerödem)
H. v. Kress and H. Langecker. *Ärtzliche Wochenschrift* [*Ärztl. Wschr.*] **1**, 5–8, July 15, 1946. 19 refs.

This article is based partly on the literature and partly on the authors' experience of hunger oedema, which occurred fairly extensively during 1946. The proximate cause of the oedema is lowering of the blood proteins, which may be due to dietary deficiency, but it also occurs after prolonged sepsis, or cachexia from various causes, in sprue, enteritis, and other conditions. Hunger oedema during 1946 was found in persons existing for many months on diets of low energy value and containing little protein. The onset was often preceded by persistent diarrhoea. The chief features of the condition are loss of weight, oedema of the face, abdomen, and upper and lower limbs, which contrast strikingly with the prominent ribs and sunken intercostal spaces; movements are slow and muscular weakness is prominent; the skin is blue-grey and pigmented in places; the pulse is slow with an increased stroke volume, and sometimes the heart is dilated; the electrocardiographic T wave is flattened; the basal metabolic rate is lowered (this is probably related to diminution in size of the thyroid and amelioration in the symptoms of Graves's disease); gastric hydrochloric acid is lowered; traces of albumin are found from time to time in the urine; pains occur in the bones and there is increased liability to fracture. In the blood the albumin is reduced but globulin is practically unchanged. The colloidal osmotic pressure is reduced to half or less than half of the normal. Water passes into the tissues and the sodium chloride content of the tissues increases. The erythrocyte sedimentation rate is raised, and in many cases the Takata-Ara reaction is positive. The ratio of arginine to lysine is disturbed. The calcium, sodium chloride and sugar contents of the blood are lowered. Excretion of creatine is increased and that of creatinine decreased. In some cases there is hypochromic anaemia which is not influenced by iron, and in some leucopenia.

In treatment, protein should be given cautiously because, as the patient has been deprived of it for so long, his digestion is likely to be upset. Milk protein is best. Niacin given by injection improves digestion and absorption. Salt-free food was not found to be effective, but blood transfusion was. Extracts of liver and of thyroid are of little use. *H. E. Magee*

DIABETES

1834. **Vitamin A and Carotene Metabolism in the Diabetic as Reflected by Blood Levels**
M. S. Kimble, O. A. Germek, and E. L. Sevringhaus. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 574–585, Nov., 1946. 1 fig., 30 refs.

High carotene values in the serum of diabetic patients have been reported, sometimes with high and sometimes with low values for vitamin A. The authors have examined samples from 116 untreated diabetics for their carotene and vitamin A content. The plasma carotene in diabetics showed a much greater scatter than in normals, and about half the values fell outside the normal range. The commonest abnormality was, however, a lowering of the plasma carotene, usually accompanied by a low vitamin A value. Only 1 patient had a high carotene level together with a low vitamin A level; therefore defective carotene conversion was unimportant

in this group of diabetics. The authors hold the view that there is no specific diabetic abnormality in carotene–vitamin A metabolism, the abnormalities observed being accounted for by non-diabetic factors. Plasma vitamin A levels in diabetics may be decreased, they suggest, by deficient intake or absorption, by acute or chronic infection, and by a low-fat diet. High values for vitamin A may be caused by renal disease; no association was found between carotinaemia and hyperlipaemia. The authors reject the concept of " diabetic carotenemia ", and attribute to a general poor nutritional status the occasional case in which a high-carotene low-vitamin-A level has been observed.

[The numerous isolated data presented in this paper show the high scatter of carotene levels in diabetics. The speculative discussion is independent of the data, and could be tested only by more detailed investigation of individual patients; in particular, the lack of information as to what diet most of the subjects of the study were taking makes the results hard to interpret.]

D. A. K. Black

1835. **Effect of Sex Hormones on Carbohydrate Metabolism in Diabetes. II. Male Hormones.** (L'azione degli ormoni sessuali sul ricambio degli idrati di carbonio nei diabetici. Nota II. Ormoni sessuali maschili)
R. MESSINA and E. ROTTINI. *Giornale di Clinica Medica* [*G. Clin. med.*] **27**, 494–507, July, 1946. 13 refs.

In a previous communication the authors described their experiments with follicular hormone in diabetes mellitus. By similar methods they then investigated the action of testosterone. Tsubura and Shiro had found no change in the fasting blood sugar in rabbits 3 weeks after castration, but there was a decrease in sugar tolerance and the rate of glycolysis in drawn blood was increased. The hyperglycaemic response to adrenaline was more marked, while glyconeogenesis and glycogenolysis proceeded more slowly. Cornil *et al.* treated diabetics with testicular hormone, noting diminution in blood sugar, glycosuria, and polyuria, and concluded that male sex hormones act not directly on the islets but through the pituitary and other endocrine organs. It has also been shown that injections of testosterone propionate cause a fall in blood sugar and muscle glycogen in guinea-pigs, and that testosterone acetate injected into dogs causes a rise in arterial blood sugar with only a minimal rise in the venous level. If, however, the suprarenal vessels are tied or the vagi or splanchnic nerves divided the same dose of testosterone produces hypoglycaemia. There was no effect in dogs after the thyroid or the pituitary gland had been removed.

In 5 diabetic subjects the authors plotted the blood sugar before and after treatment with testosterone. Curves were obtained of blood sugar measured half-hourly for 4 hours after giving (*a*) 40 g. glucose by mouth, (*b*) 1 mg. adrenaline subcutaneously, and (*c*) 20 units of insulin, before and after dosage with 10 mg. testosterone propionate daily by intramuscular injection for 5 days. In each case the first blood sugar was taken after a 16-hour fast. In 2 cases before treatment glycaemic curves were obtained after the injection of 50 mg. of testosterone. After the course of injections of male sex hormone capillary and venous blood sugar fell, the former from an average of 289 to 189 mg. per 100 ml. and the latter from 280 to 175 mg., the capillary-venous difference increasing from 9 to 14 mg.; this denotes increased peripheral utilization of glucose. The adrenaline response was less marked after testosterone, the curve being much flatter. The testicular extract had little effect on insulin hypoglycaemia. In the 2 cases investigated male sex hormone caused a fall in fasting blood sugar—in one from 210 to 95 mg. per 100 ml. after 3 hours and in the other from 267 to 181 mg. in 2½ hours. The authors conclude that male sex hormone (as was the case with female hormones in their previous experiments) has a beneficial effect in diabetes mellitus, reducing the fasting blood sugar and improving the peripheral utilization of glucose, and probably acting through the endocrine and vegetative nervous systems rather than by direct effect on liver and muscle cells.

E. G. Sita-Lumsden

1836. **The Classification of Cases of Glycosuria**
A. LYALL. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **15**, 243–253, Oct., 1946. 2 figs., 15 refs.

In 387 cases of incidental glycosuria the venous blood sugar was determined by Maclean's method in the fasting state and at ½-hourly intervals for 2 hours after the ingestion of 50 g. glucose. Urine specimens obtained on waking, in the fasting state, and 2 hours after glucose had been taken were tested for sugar and ketones. [Unlike the standard procedure, this test gives no precise indication of the threshold level or the contribution to glycosuria made by a low leak point in cases where there is also a transient hyperglycaemia.] Of these cases, 41 were classified as diabetic or in the " prediabetic state ", 112 as " doubtfully diabetic ", 159 as renal glycosuria with blood sugar curves rising up to 0·15 g. per 100 ml., 52 as renal glycosuria with blood sugar curves up to 0·12 g. per 100 ml., and 23 as renal glycosuria with low values of the blood sugar and persistent glycosuria even at fasting levels of the blood sugar. [The author pleads that the cases in the last group should be labelled as " renal diabetes ", but many will prefer to regard renal glycosuria as a physiological aberration varying in degree, and of slight clinical significance.]

H. Whittaker

1837. **Lack of Response to Insulin.** Report of a Patient Treated with Five Thousand Units per Twenty-four Hours
L. S. SMELO. *Southern Medical Journal* (*Sth. med. J., Nashville*) **40**, 333–340, April, 1947. 21 refs.

1838. **Antagonism of the Diabetogenic Action of Alloxan by Pentnucleotide in the Rat**
G. A. EMERSON, P. L. EWING, and T. B. THOMAS. *Texas Reports on Biology and Medicine* [*Tex. Rep. Biol. Med.*] **4**, 452–469, Winter, 1946. 10 figs., 17 refs.

Cardiovascular Disorders

1839. **Acute Pericarditis Simulating Coronary Artery Occlusion**
C. W. COFFEN and M. SCARF. *American Heart Journal* [*Amer. Heart J.*] **32**, 515–518, Oct., 1946. 1 fig., 12 refs.

A clinical report is given of a case of intense substernal pain of sudden onset in a previously healthy 26-year-old male. During examination the patient was pale and cyanosed, and the blood pressure, which initially was 120/80 mm. Hg, became too low to measure, while the pulse rate fell from 72 to 38 per minute. Gradual recovery followed the administration of morphine and oxygen. Fever, leucocytosis, an increased erythrocyte sedimentation rate, and a transient friction rub also developed, but disappeared after about 48 hours. The further course was uneventful. Because of several features, such as the age of the patient, the aggravation of the substernal pain by breathing and change of position, and the electrocardiographic findings, the case is interpreted as one of acute pericarditis of unknown cause, and not as one of coronary thrombosis.

R. T. Grant

1840. **Myocardial Lesions due to Starvation.** (Myokardschaden bei Inanition)
R. FORSTER. *Cardiologia* [*Cardiologia, Basel*] **10**, 369–378, 1946. 4 figs., 6 refs.

This paper describes the clinical, post-mortem, and electrocardiographic changes in 31 cases of starvation from German concentration camps. The most frequent electrocardiographic finding was a reduction in amplitude of the deflections, particularly of the T wave. At necropsy the most frequent cardiac change found was fatty degeneration of the myocardium. In these cases recognizable vitamin deficiencies were seldom seen, though infections and pre-existing cardiac abnormalities were frequent. The mechanism of the changes seen is discussed.

H. E. Holling

1841. **The Relation between Circulation Time and the Amount of the Residual Blood of the Heart**
B. GERNANDT and G. NYLIN. *American Heart Journal* [*Amer. Heart J.*] **32**, 411–418, Oct., 1946. 2 figs., 17 refs.

The authors have measured the " circulation time ", the " heart volume ", and the brachial venous pressure in 308 patients with heart disease. In 214 of the patients the heart lesion was compensated and in 94 it was decompensated, as evidenced by oedema, a palpable liver and spleen, and pulmonary congestion. The venous pressure was measured with the patient flat on his back. A cannula with an inside diameter of 0·9 mm. was inserted into the antecubital vein and connected to a graduated tube. Heparin was used as an anticoagulant. The circulation time was measured by injecting 5 ml. of a 20% solution of dehydrocholic acid as quickly as possible through the cannula and noting the time of appearance of a bitter taste. The determinations of heart volume were made by an *x*-ray technique described by Lysholm *et al.* (*Acta radiol.*, 1934, **15**, 237) and for reasons given elsewhere the present authors regard the heart volume so determined as indicating " the amount of residual blood of the heart ".

They find in all cases a significant relation between the heart volume and the circulation time. They also state that " the studies have clearly proved that, above all, the circulation time depends on the amount of residual blood in the heart and only to a slight extent on the degree of decompensation, i.e., of congestion ".

Correlation	Number	$r \pm O_r$
Volume (V/M^2)–circulation time ..	93	$0{\cdot}37 \pm 0{\cdot}090$
Volume (V/M^2)–venous pressure ..	93	$0{\cdot}37 \pm 0{\cdot}090$
Venous pressure–circulation time ..	94	$0{\cdot}39 \pm 0{\cdot}088$

[This last statement does not seem to be borne out by the correlation coefficients given for relative heart volume, circulation time, and degree of decompensation, measured by the venous pressure, as shown in the table.]

H. E. Holling

1842. **Electrocardiographic Phenomena Associated with Spontaneous Pneumothorax and Mediastinal Emphysema**
D. LITTMANN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 682–690, Dec., 1946. 6 figs., 17 refs.

Two young soldiers who had been suddenly taken ill with severe precordial pain and were found to be suffering from mediastinal emphysema and left-sided pneumothorax showed interesting electrocardiographic changes. These were mainly confined to the chest leads, and were only observed when the electrocardiogram was taken with the patients in the supine position, but not in the erect and prone positions, in which the patients were more comfortable. The electrocardiographic changes are strikingly illustrated in records obtained with the patients on a radiographic tilting table on which they were rapidly moved from the supine to the erect position and back again: the T waves (leads CF3 and 4 respectively) gradually changed from an inverted to an upright and back to an inverted form. No electrocardiographic changes were observed after the resorption of the mediastinal emphysema, " though the pneumothorax took a little longer to disappear completely ". Discussing the findings the author dismisses the explanation that the changes in the electrocardiogram were caused by an impairment of the coronary circulation, and in his opinion the increased amount of air between heart and sternum in the supine position, as evidenced by

radiographs, interfered with the conduction between the heart and the exploring electrode and thus was responsible for the abnormality in the chest leads. In this connexion the observations of Katz and his associates, who could produce marked deviations from the normal electrocardiogram by inserting rubber dams between the heart and its surrounding tissues, are adduced.

In a postscript a third similar case, observed after the paper had been submitted for publication, is briefly mentioned. *B. Samet*

1843. **Effect of Antimony on the Electrocardiogram**
E. F. SCHROEDER, F. A. ROSE, and H. MOST. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **122**, 697–706, Dec., 1946. 5 figs., 7 refs.

The extensive use of antimony preparations in the treatment of schistosomiasis and leishmaniasis, and, to a lesser degree, of filariasis, revived the interest in an earlier report by Mainzer and Krause (*Trans. R. Soc. trop. med. Hyg.*, 1939, **33**, 405), who had observed sudden deaths during antimony therapy. In a series of 14 schistosomiasis patients, 3 had shown marked, 4 suspicious, and 2 insignificant, changes of the S–T intervals and T waves. Tarr (*Bull. U.S. Army med. Dept.*, 1946, **5**, 336) observed changes in the T waves in 80% of 66 patients treated with antimony for schistosomiasis. The authors studied the electrocardiograms in 100 patients who underwent treatment for infections with *Schistosoma japonicum* and *S. mansoni*. The drugs used were "fouadin", 70 or 100 ml. in 27 and 14 days respectively (a total of 0·599 g. and 0·870 g. of antimony), or tartar emetic in 0·5% solution in 10% glucose, 1·45 g. in 31 days or 1·8 g. in 29 days (0·522 g. and 0·648 g. of antimony respectively). No symptoms or signs of cardiovascular disease were observed before, during, or after treatment, and no fatality occurred. The most constant and striking change was noted in the T waves, which in 99% showed a decrease, flattening, or inversion; these changes were more marked in treatment with tartar emetic than with fouadin. Fusion of the S–T segment with the T wave was found in 45%, and changes of the P waves in 11%. The duration of the systole (Q–T interval), calculated by the formula $Q\text{–}T = K\sqrt{RR}$ (Cheer and Dieuaide, *J. clin. Invest.*, 1931, **10**, 890) was prolonged in 27%. The changes lasted up to 2 months after the conclusion of the treatment. The aetiology and significance of the electrocardiographic changes during antimony therapy are not known, but the authors do not regard them as "indicative of cardiac damage or serious impairment of cardiac function". *B. Samet*

1844. **The T Wave of the Precordial Electrocardiogram at Different Age Levels**
R. M. SUAREZ and R. M. SUAREZ, JR. *American Heart Journal* [*Amer. Heart J.*] **32** 480–493 Oct., 1946. 7 figs., 119 refs.

Inverted T waves occur in the precordial electrocardiograms of normal subjects up to 15 years of age. The present observations were made to determine the incidence of these findings in various age groups in 161 healthy Puerto Ricans aged 5 to 46 years. With the exploring electrode paired with the arm and leg leads through a central terminal, records were taken from the six classical chest positions (C.V.1 to C.V.6). In the youngest subjects up to 12 years old, inverted or diphasic T waves were found as far laterally as position 5, in subjects 12 to 18 years of age as far as position 4, and in adults as far as position 3. The results suggest that, irrespective of age or sex, a negative T wave in C.V.6 may be regarded as abnormal, while the same finding in C.V.1 may be normal. Negative T waves in C.V.4 or C.V.5 are probably abnormal over 12 years of age.
W. J. H. Butterfield

1845. **Cardiac Muscle. Further Studies; Investigation of Chemical Changes in Myocardial Insufficiency with Special Reference to Adenosinetriphosphate**
G. H. MANGUN and V. C. MYERS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 441–446, Oct., 1946. 12 refs.

The creatine, the total phosphorus and acid-soluble phosphorus, and possibly the potassium content of a failing heart muscle are usually decreased. In the dog with myocardial insufficiency due to induced aortic incompetence, Mangun and Roberts had noted a marked decrease in the adenosine-triphosphate and phosphocreatine content of the left ventricle. The present authors use a new method for the estimation of total acid-soluble purines and of oxypurines, which involves hydrolysis of purine compounds, de-amination with nitrous acid, precipitation with copper bisulphite, and estimation of the nitrogen content of the precipitate. They claim that the acid-extractable purine content of the left ventricle, calculated as adenine, is decreased in myocardial insufficiency. Lowered concentrations of purine were also observed in the myocardium of the right ventricle in some, but not in all, cases of pneumonia.

[The method here used for the determination of purines has not been adequately tested for its specificity, as the authors admit. Nor, in spite of the control series, does it appear that due consideration has been given to the effects of post-mortem autolysis or to the fact that the cardiac changes may not be specific for this muscle but may simply form part of the general congestive tissue changes which ensue with prolonged myocardial insufficiency.] *Henry Cohen*

1846. **Diet Low in Salt (Sodium) in Congestive Heart Failure**
E. O. WHEELER, W. C. BRIDGES, and P. D. WHITE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 16–20, Jan. 4, 1947. 3 figs., 13 refs.

One of the most important changes associated with heart failure is an increase in volume of the circulating blood. This tends to be particularly distributed in the venous circulation and seems to be associated with a rise in venous pressure. There is no doubt that in many cases of heart failure retention of sodium by the kidney occurs quite early. This is associated with an increase in the patient's weight, probably due to increase in the

extracellular tissue fluid. There is *pari passu* with the retention of sodium a retention of water. This state of affairs soon leads to the development of oedema. It would appear that oedema can be precipitated by feeding sodium chloride to patients who have a mild degree of heart failure.

As a result of these phenomena the treatment of oedema has been developed with particular attention to the elimination of sodium from the diet as much as possible. In the past it has been customary to restrict the fluid intake, often severely, and it was only too common to see a patient complaining bitterly of thirst, with a dry tongue, and yet hopelessly waterlogged below the waist. If a diet low in sodium is given, it is possible to allow a fluid intake dictated by the patient's taste. Some even suggest that the intake of fluid should be pushed, but this is probably unnecessary and can be left to the patient. The average diet. without salt added at table, contains about 4 to 7 g. of sodium chloride; without salt added in cooking, it contains 3 to 4 g.; a low-sodium diet contains 1·5 to 2 g. of sodium chloride. The chief difference between the last two lies in the use of salt-free bread and butter. It is important in this diet to avoid sodium in any form, such as baking powder and some salt substitutes which contain sodium. Butter must be washed free from salt, and salt-free bread must be prepared. Cheese as a rule contains a fair amount of salt, with the exception of cream cheese. No drugs containing sodium should be given. On this diet, with the help of occasional mercurial diuretics, or even without them, a patient can become free from oedema and remain so. The disadvantage is in the tasteless food. Potassium and ammonium chloride are a somewhat poor substitute for sodium chloride in imparting some flavour.

[It may be difficult, particularly in Britain, to achieve such a diet in these times, but it can be successful and is worth a trial when patients fail to lose their oedema under treatment with diuretics. It certainly has the great advantage of allowing a fairly free intake of water.]

Terence East

1847. **Effect of Quinidine on the Circulatory System.** (Algunos efectos de la quinidina sobre el aparato circulatorio)

J. García Ramos and B. Peraltar. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **16**, 302–310, July 30, 1946. 2 figs., 4 refs.

This study is concerned with the effects on the circulatory system of doses of quinidine smaller than those employed therapeutically and their relation to these effects. Cats were anaesthetized with allobarbitone (0·7 ml. per kilo). In one group the arterial pressure was measured by means of a cannula in a carotid artery, and electrocardiographic records were made, the electrodes being on the right forefoot and the epigastrium. Electrodes were also placed on the left vagus and a sciatic nerve for faradic stimulation, both nerves being cut distally. In a second group the heart was exposed; electrodes were placed in both auricles and both ventricles, and the electrical changes were recorded after amplification.

In the first group were observed the effects on the heart rate, conductivity and response to vagal and sciatic stimulation, of compression of the carotid and of adrenaline injection. In the second group the effects of injecting intravenously a solution of quinidine sulphate 1/200, 0·25 to 10 mg. per kilo, on auricular response to moderate and high frequencies were noted. It was observed that there was no effect on the heart rate with 0·25 mg., but steady reduction and more prolonged effect were seen as the dose increased. As regards conduction, the P–R interval was increased with doses above 0·5 mg., the increase and its persistence being proportionate to the dose. A depression of blood pressure was apparent with 0·5 mg., and again varied directly with the dose. Reflex variations in rate from stimulation of the sciatic or from carotid compression were not appreciably influenced by doses under 5 mg. per kilo, but with this dose and above the variations were diminished and finally abolished. In some cases the central stimulation of the left vagus caused a fall in arterial pressure and a reduction in heart rate; quinidine in doses of 0·5 mg. per kilo and above diminished these effects. The response to adrenaline was not influenced by quinidine in doses smaller than 0·5 mg., but was diminished with larger doses. The duration of these effects varied directly with the dose, being 5 to 10 minutes with 0·5 mg. per kilo and 1 hour or more with 10 mg. In the cat, when the rate of auricular stimulus is 8 per second a 2 : 1 block appears. With 9 per second and above the auricle does not respond unless the strength of the stimulus is increased. Auricular flutter was never obtained. Under quinidine a prolongation of the P–R interval was seen to occur with a lower rate of stimulus than without quinidine, and similarly heart-block occurred with lower frequencies; there was an increase in the next three or four P–R intervals after the stimulus had ceased. The possibility that these results were caused by fatigue was excluded. In some cases it was noted that the threshold to stimulation was raised after quinidine.

The authors conclude that even minimal doses of quinidine produce proportionate effects on the power of recovery of the circulatory system, a diminution in sensibility both to electrical stimuli and to adrenaline, and a decrease in the heart rate. As regards arterial pressure, small doses depress vasomotor reflexes, but direct effects both on blood vessels and on nerve centres are apparent only with larger doses, when the respiratory centre may also be affected. They confirm Lewis and Dale's observations (*Heart*, 1922, **9**, 55, 87) that quinidine reduces the cardiac inhibition which normally follows central stimulation of the left vagus. *J. J. Keevil*

1848. **Bacterial Endocarditis of the Tricuspid Valve**

L. Karotkin and P. Marcuse. *Southern Medical Journal* [*Sth. med. J.*] **39**, 769–774, Oct., 1946. 3 figs., 28 refs.

The authors draw attention to the difficulty of diagnosing bacterial endocarditis involving only the right side of the heart; signs of organic heart disease are often lacking, the blood culture usually remains negative, and systemic embolism fails to appear unless tissue

breakdown occurs in the lungs. They report 3 cases of bacterial endocarditis of the tricuspid valve, giving necropsy findings in each case. Case 1 had a tricuspid valve already damaged by rheumatism; early blood culture was negative, but later pneumococcus Type VII was grown from venous blood. In Case 2 the endocarditis complicated lobar pneumonia, and the sputum contained Type VII pneumococcus; blood culture was not performed. In Case 3 the valvular lesion occurred in the course of a *Staphylococcus aureus* septicaemia, and blood culture was repeatedly positive. From their study of the literature the authors conclude that acute bacterial endocarditis of the tricuspid valve alone is rare, and subacute bacterial endocarditis of this valve is even more rare. On the other hand, involvement of the tricuspid valve in addition to other valves is " perhaps not quite so rare as is commonly believed ". Although bacteriaemia is less common in bacterial endocarditis confined to the right side of the heart, quite a number of instances have been reported; this can be attributed to the presence of lesions in the lungs of such a nature that their filtering action is impaired. " Positive blood cultures or even the presence of an occasional embolus in the systemic circulation should therefore not rule out the diagnosis of tricuspid or pulmonary endocarditis."

D. A. K. Black

1849. **A New Case of " Bloc bilatéral manqué ".** (Nouvelles recherches sur le " bloc bilatéral manqué ")
F. Addarii, L. Martini, I. Mahaim, and M. Winston. *Cardiologia* [*Cardiologia, Basel*] **11**, 36–59, 1946. 16 figs., 21 refs.

This work is divided into two parts: the first deals with the clinical study by Addarii and Martini; the second is a histo-pathological investigation by Mahaim and Winston. It is concerned with a case of idiopathic familial cardiopathy, presenting progressive congestive heart failure, with cardiac enlargement, irregular bradycardia, ventricular extrasystoles, and auricular fibrillation. The pathogenesis of this myocardial disorder is explained on the basis of " bloc bilatéral manqué " [a suitable English translation would be " missed bilateral bundle-branch block "]. Mahaim as far back as 1932 published a paper in which he showed that destruction of both bundle branches may be associated with non-existence of auriculo-ventricular block; hence the term " missed bilateral bundle-branch ".

The present case is of a man aged 29 years who presented progressive myocardial failure since the age of 14. He had a brother suffering from a similar disorder (the latter will be the subject of a separate paper to be published later). The illness started with the onset of irregular bradycardia, the heart rate averaging 40 per minute. Syncopal attacks were also noted in the first few years. At the age of 28 complete heart failure of the congestive type supervened; oliguria, anasarca, dyspnoea, swelling of jugular veins, engorgement of the liver, and prolongation of the circulation time (58 seconds with dehydrocholic acid) were the main features. The patient was first investigated in 1937, when the heart rate varied between 28 and 31 beats per minute. The electrocardiogram showed auricular fibrillation, arrhythmic bradycardia, occasional ventricular extrasystoles without compensatory pauses, and QRS complexes suggestive of bundle-branch block with a duration of 0·20 second. These features of QRS complexes are characteristic in " bloc bilatéral manqué ". The heart was much enlarged and globular in form. Treatment was of no avail, and the patient died nearly 3 months after admission to hospital. During the last 72 hours he presented an S_1R_3 type of ventricular tachycardia (160 beats per minute). At necropsy the heart muscle showed disseminated foci of fibrosis with at places lymphoplasmocytic infiltration. There was no evidence of systematized arterial disease, nor was perivascular cellular infiltration seen. Mahaim and Winston prepared 4,580 slides of the myocardium and systematically examined 1,400 of them, thus being able to trace the whole of the specialized conducting cardiac tissue, and, in particular, to investigate the A–V node, common bundle, and its branches. This painstaking study showed that Tawara's node and the bundle of His were intact, but the A–V node was completely isolated from the auricular myocardium by areas of scar tissue. An area of the left bundle branch 2 cm. long was completely destroyed as well as the interseptal portion of the right bundle branch; the latter also showed complete interruption at the lower third. All these lesions of the conducting system seemed to be due to an old healed myocarditis, which produced diffuse fibrosis, especially noticeable in the interventricular and interauricular septa. However, the most important finding was the presence of specialized tissue, forming independent conducting connexions between the A–V node and the bundle of His on the one hand, and the ventricular septal myocardium on the other. The authors conclude that this is not a case of ordinary A–V block; although the two bundle branches are interrupted and unable to transmit the wave of excitation from the A–V node, the latter nevertheless spreads to the interventricular septum through the intermediary of the high connexions found histologically. This is the mechanism designated " bloc bilatéral manqué ". The long duration of QRS is due to the fact that the excitation wave takes a longer time to pass through septal myocardium than specialized conducting tissue. They consider it to be a case of nodal rhythm, the A–V node remaining the pace-maker.

According to the authors, it would seem that, as a general rule, high-situated connexions of conducting tissue nearly always exist in man, and that in case of injury to the bundle branches these may serve as a relay between the A–V node and the interventricular septum.

A. I. Suchecki

1850. **Cardiac Failure in Cattle on Vitamin E-free Rations as Revealed by Electrocardiograms**
T. W. Gullickson and C. E. Calverley. *Science* [*Science*] **104**, 312–313, Oct. 4, 1946. 1 fig., 5 refs.

The electrocardiogram is given of a heifer that died suddenly at 21 months as a result of being raised on vitamin-E-free rations. The changes consisted of an increased P–R interval, QRS changes indicative of axis

deviation and later of widening, and extrasystoles. The authors consider that this is evidence of a decreased functional activity of the myocardium. Microscopically, atrophy and scarring of the cardiac muscle fibres were clearly indicated, together with an increase in the cellular elements, which in some instances strikingly resemble small Aschoff nodules. *S. Oram*

1851. **Coronary Sinus Rhythm**
D. SCHERF and R. HARRIS. *American Heart Journal* [*Amer. Heart J.*] **32**, 443–456, Oct., 1946. 5 figs., 30 refs.

In the course of 23,610 routine electrocardiographic examinations 31 cases of coronary sinus rhythm were diagnosed by the low positive or absent P waves in lead I, deep, inverted, and usually peaked P waves in leads II and III, and a normal or slightly shortened P–R interval. These changes were previously observed by Scherf in dogs after warming the coronary sinus *in situ*. The cases were evenly distributed between the sexes, and the majority of patients showed evidence of heart disease. The rhythm was very labile and changed spontaneously or after exercise, amyl nitrite inhalations, or carotid sinus pressure. As the authors point out, it should be noted that, in our present state of knowledge, it is not possible to differentiate between rhythms originating in the region of the coronary sinus and in the upper part of the auriculo-ventricular node. *W. J. H. Butterfield*

1852. **Study of the Electrocardiogram in Auriculo-Ventricular Block.** (Étude de l'électrocardiogramme dans le bloc atrio-ventriculaire)
G. FATZER. *Cardiologia* [*Cardiologia, Basel*] **10**, 305–368, 1946. 13 figs., 72 refs.

Forty-four cases of total A–V block were studied (19 men, 25 women). Arteriosclerosis and rheumatic myocarditis were the main causes. Arteriosclerosis is more liable to produce intermittent block than myocarditis. The prognosis of A–V block depends on the condition of the myocardium, the frequency of Adams-Stokes attacks which carry a bad prognosis, the presence of bundle-branch block, and the length of the Q–T interval. Sinus arrhythmia, blood pressure, haemoglobin values, cardiac enlargement, observed in most cases, and decompensation present in 50% of the cases, were studied in detail. *H. E. Holling*

1853. **Abnormalities of the Respiratory Pattern in Patients with Cardiac Dyspnea**
H. E. HEYER. *American Heart Journal* [*Amer. Heart J.*] **32**, 457–467, Oct., 1946. 5 figs., 18 refs.

The movements of the chest wall during respiration were recorded from a Marey pneumograph on to a kymograph drum. In this way the "respiratory pattern" was studied in 5 normal subjects, 11 cases of cardiac disease with clinical pulmonary congestion, and in 2 cases of allergic asthma during the attacks. In the last two groups of subjects the tracings confirmed the presence of a prolongation of expiration and showed a terminal slowing in this phase. After exercise these cases did not show the relative shortening of expiration, as compared with inspiration, which was seen in the normal subjects. However, after receiving 0·5 g. of aminophylline intravenously, 5 out of 6 cases of pulmonary congestion and both cases of asthma showed faster breathing, presumed to be of central origin, with greatly increased vital capacity and shortening of the expiratory phase without terminal slowing, which in the author's opinion is due to the relaxation of bronchospasm. *W. J. H. Butterfield*

1854. **Some Observations on the Pathogenesis of Edema in Cardiac Failure**
F. REICHSMAN and H. GRANT. *American Heart Journal* [*Amer. Heart J.*] **32**, 438–442, Oct., 1946. 1 fig., 15 refs.

Observations were made on 3 patients with rheumatic heart disease and auricular fibrillation, treated with digitalis. All 3 patients had had repeated attacks of cardiac failure, in 2 of them associated with oedema. When in hospital on a diet containing about 3 to 4 g. of sodium chloride the digitalis was withdrawn, and the venous pressure (measured directly) in these patients rose before there was formation of oedema.

[The authors argue, but do not show, that the main factor in the production of cardiac oedema is increased venous pressure.] *E. B. G. Reeve*

1855. **Congenital Cardiovascular Malformations. Discussion of Some of the More Common Types**
L. L. LIPSCOMB and W. W. ANDERSON. *Journal of the Medical Association of Georgia* [*J. med. Ass. Ga*] **35**, 273–280, Oct., 1946. 9 figs., 12 refs.

Accurate diagnosis of the type of anomaly in congenital heart disease is important in view of the development of surgical procedures to correct or modify abnormalities. Good brief accounts are given of the more common types of lesion, but nothing new is added to the literature except in regard to anomalies of the aortic arch. These are often of no clinical significance, as in the case of persistent right aortic arch with right descending aorta. If there is a right aortic arch and left descending aorta then the arch lies posterior to the oesophagus and trachea and symptoms such as brassy cough, dyspnoea, dysphagia, and recurrent attacks of bronchitis or bronchiolitis are produced. The condition can be diagnosed radiologically with a barium "swallow". In the lateral radioscopic view the oesophagus can be seen to be angulated forwards by the aorta passing behind. In the antero-posterior view there is a prominence of the great vessels on the right and an absence of their shadow on the left. A filling defect is usually noted in the oesophagus at the level of the fourth and fifth thoracic vertebrae and the viscus is displaced slightly to the left.

A similar but more severe set of symptoms is produced by the presence of a vascular ring enclosing the trachea and oesophagus. This is usually due to the persistence of both right and left aortic arches. A case is reported in an 11-months-old baby. The findings differed from those in a case of simple persistent right aortic arch with left descending aorta in that (1) in the antero-posterior view the oesophagus was in the midline, and (2) a

" lipiodol " bronchogram demonstrated concentric constriction of the trachea at the level of the oesophageal angulation. Exploration was made and the small left aortic arch was ligated and divided. There was clinical improvement but some stridor persisted.

F. A. Langley

1856. **Cardiovascular Defects in Selective Service Registrants**

R. H. EANES, K. H. MCGILL, and M. L. CLARK. *American Heart Journal* [*Amer. Heart J.*] **32**, 504–514, Oct., 1946. 4 refs.

Cardiovascular defects were the fourth most important cause for rejection of men liable for military service, accounting for 6·7% of the total rejects. In this group valvular disease of the heart was the most common cause (44·1%), followed by hypertension (31·6%), although in negroes the two types of cardiac affection were equally important (40%). The diagnosis of rheumatic heart disease was made three times more commonly in white subjects than in negroes. Hypertension became more important as a cause of rejection with increasing age, particularly in negroes, in whom it was the cause of three-fourths of the rejections due to cardiovascular defects in men aged 30 years or over. *B. McArdle*

1857. **The Treatment of Angina Pectoris by Irradiation of the Adrenal Glands; Clinical Experience**

R. L. MCMILLAN and J. P. ROUSSEAU. *North Carolina Medical Journal* [*N.C. med. J.*] **7**, 550–553, Oct., 1946. 10 refs.

The adrenal glands of 23 patients with severe angina pectoris were irradiated, each adrenal area receiving 600 r in three divided doses over a week. Thirteen patients were greatly relieved, 4 moderately so, 3 slightly, and 3 not at all. The period of observation was 2 to 12 months. Two of the patients who most benefited died suddenly during this time, and a third died from probable myocardial infarction. Blood pressure readings did not change significantly in the males, but showed an average drop of 23/22 mm. Hg in the females. On the whole, patients seemed less emotional after treatment. The most severe cases, and those in which attacks were especially provoked by emotion, did best. The subsequent incidence of myocardial infarction and the life expectancy are assumed to remain unaltered.

Paul Wood

1858. **Disadvantages of Thiouracil Treatment of Angina Pectoris**

J. R. DIPALMA and J. J. MAGOVERN. *American Heart Journal* [*Amer. Heart J.*] **32**, 494–503, Oct., 1946. 4 figs., 16 refs.

Eight patients with angina pectoris who had been under observation for several years were given thiouracil (usually 0·6 g. daily) for periods ranging from 3 weeks to 14 months. The effects on their anginal pain, exercise tolerance, and basal metabolic rate were studied. Difficulty was experienced in lowering the basal metabolic rate to the optimum level of −10 to −20%, at which levels the anginal pain was less severe; below these levels the patients became too myxoedematous. The authors believe that there is a tendency for water retention to occur as the metabolism is lowered, so that pulmonary oedema and increased dyspnoea appear. Two patients developed toxic skin rashes. Four of them benefited from the thiouracil, but in only 2 of these was the improvement marked. Both of these had a raised basal metabolic rate before treatment, a finding which is considered the only indication for use of the drug other than as a therapeutic test in the selection for thyroidectomy of patients with angina pectoris. *B. McArdle*

1859. **The Influence of Age on Blood Pressure. A Study of 5,331 White Male Subjects**

H. I. RUSSEK, M. M. RATH, B. L. ZOHMAN, and I. MILLER, *American Heart Journal* [*Amer. Heart J.*] **32**, 468–479, Oct., 1946. 3 figs., 26 refs.

A statistical analysis of the systolic and diastolic blood pressure readings of 5,331 white males between the ages of 40 and 95 years is presented. The subjects were observed in two service hospitals and two institutions for aged people. The gist of the findings is that a systolic blood pressure below " 100 plus the age " is " normal ", and a diastolic blood pressure of over 90 mm. Hg is abnormal at any age. *H. E. Holling*

1860. **Treatment of Thromboangitis [*sic*] Obliterans by Roentgen Therapy. Report of a Case**

U. V. PORTMANN and G. E. PARSONS. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **13**, 237–240, Oct., 1946. 3 refs.

A single case is recorded of a patient said to have thrombo-angiitis obliterans who was first seen in December, 1932, and when last seen, in June, 1946, " had been free from symptoms and signs of the disease for 13 years apparently as a result of roentgen irradiation directed to the spinal sympathetic ganglia ", from " the first thoracic to the third lumbar segments ".

[There are many difficulties in accepting the authors' conclusion in this case. The detailed record throws doubt on the diagnosis. The patient, a man of 37, had a blood Wassermann reaction of ++++ and was given antisyphilitic treatment without apparent early response; arterial pulsation was absent from the dorsalis pedis and posterior tibial arteries, and after spinal analgesia which produced " anaesthesia to the level of the nipples " the rise in temperature of the left big toe was from 83° to 83·1° F. (28·33° to 28·4° C.). Yet in June, 1946, the arterial pulse had returned to the dorsalis pedis arteries and the left big toe temperature was 87° F. (30·55° C.) without spinal analgesia. The wide variations in the natural course of thrombo-angiitis obliterans (I have seen cases similar to that here recorded in which spontaneous cure has occurred) and the possibility of a syphilitic element in the endarteritis, throw doubt on the part played by *x*-ray treatment in this patient's recovery.]

Henry Cohen

Disorders of the Blood

1861. **The Genesis of Ehrlich's Mast Cells.** (Beitrag zur Frage der Genese der Ehrlichschen Mastzellen)
H. HOLMGREN. *Acta Anatomica* [*Acta anat.*] **2**, 40–56, 1946. 6 figs., 27 refs.

The author reviews various suggestions which have been advanced concerning the genesis of mast cells in foetal and postnatal life. He has himself re-investigated the problem, using a fixative containing basic lead acetate because this salt precipitates heparin. His material consisted of a series of human and mammalian foetuses (cat, rabbit, rat) of varying ages. All were fixed in basic lead acetate, cut in serial section, and stained with 1% toluidine blue. In this study mast cells have not been detected in human foetuses of less than 9 cm. crown–heel length. They are first found in the subcutaneous tissue of the fingers and in the submucosa of the gut. Two types can be distinguished at this and all later stages: (*a*) a cell with a large hypochromatic nucleus resembling that of the mesenchyme cell, and with cytoplasm containing fine and markedly metachromatic granules situated mainly peripherally; and (*b*) a cell with a small dark highly chromatic nucleus resembling that of a lymphocyte. With advance in the age of the foetus the number of mast cells increases, especially in the connective tissues. The lungs, kidneys, and adrenals possess no mast cells until the end of foetal life, probably through late development of connective tissue in these organs.

Mast cells, at the time of their first appearance, are not found in close proximity to blood vessels or to collections of lymphocytes. They are rare in the spleen. There was nothing to suggest that mast cells could be developed from clasmatocytes or plasma cells. Mesenchyme cells can be found with nuclei closely resembling the nuclei of both types of mast cell. Moreover, mast cells of type *a* become more numerous in older foetuses. Probably the two types represent cells of different ages. It is perhaps significant that in the 9-cm. human foetus definite mesenchyme cells which contain metachromatic granules occur. These may represent pro-mast cells. The findings in other mammalian embryos were essentially similar. The author concludes that mast cells develop directly from the mesenchyme, and not from endothelial cells, lymphocytes, or monocytes. They are highly specialized cells, following their own line of development and separating at an early stage into two distinct types. They probably have a special function. *H. Hughes*

1862. **Capillary Microscopy with Special Reference to Capillary Petechiae**
E. DAVIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 192–196, Aug., 1946. 10 figs., 6 refs.

" Petechiae " were frequent in arteriosclerosis, purpura simplex, scurvy, bronchiectasis, Raynaud's disease, and clubbed fingers; they were not found in healthy people, but were discovered in such diverse conditions as infective hepatitis, gout, syphilis, and " various diseases of the heart, lung, kidney, nervous system, blood and skin ".

[The author does not describe his technique for capillary microscopy (since it has been previously described); he recommends the technique as a " gratifying and stimulating occupation for the observer ". It is not always clear, however, that the appearances which he describes as petechiae were in fact extravasations of blood outside the capillary wall, for he talks of the capillary " reattaching itself to the petechia ", and one is led to suppose that some of his " petechiae " may in fact have been stagnant blood within capillaries. This reservation lessens the value of his observations on the nail beds of 1,000 patients, when he found " capillary petechiae " in 100 of 533 consecutive patients.] *H. E. Holling*

1863. **Vitamin Levels in Pernicious Anemia**
D. CAYER, J. M. RUFFIN, and W. A. PERLZWEIG. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 197–184, Aug., 1946. 6 figs., 12 refs.

Few quantitative studies have yet been reported concerning the presence or absence of vitamin deficiencies in pernicious anaemia. The present paper gives the results of such a study in 7 cases of pernicious anaemia during relapses and 1 in a stage of remission. Observations were also made on a group of 25 cases of vitamin-B-complex deficiency and on a control group of 30 healthy medical students.

All the subjects were studied in hospital. They were placed on a standard diet of which the estimated vitamin content was known. Plasma vitamin A was determined by Kimble's method, and vitamin C by the technique of Mindlin and Butler (*J. biol. Chem.*, 1938, **122**, 673) using Tillman's dye. The vitamins of the B complex were determined in the urine before and after the following test doses: thiamine 1 mg. intramuscularly; riboflavin 5 mg. orally; nicotinic acid amide 500 mg. orally; pyridoxine 50 mg. orally. Thiamine was determined by the yeast fermentation and thiochrome methods; riboflavin by the direct fluorometric method of Ferrebee (*J. clin. Invest.*, 1940, **19**, 251), omitting the absorption and elution steps; nicotinic acid by the load test of Perlzweig, Sarett, and Margolis (*J. Amer. med. Ass.*, 1942, **118**, 28); pyridoxine colorimetrically by the technique of Scudi, Buhs, and Hood (*J. biol. Chem.*, 1942, **142**, 323).

The results are summarized in the accompanying table taken from the authors' paper. It is concluded that the pernicious anaemia group was significantly deficient in thiamine, nicotinic acid, and riboflavin, and that these results justify the administration of B-complex vitamins

to patients having pernicious anaemia if liver extract alone fails to produce a satisfactory response.

Arithmetical Means of Vitamin Levels

Vitamins *	Student controls	B-complex deficiencies	Pernicious anaemia patients	Suggested lower limit of normal
A	114	89	85	75
Carotene	265	205	154	165
C	0·67	0·33	0·42	0·15
Nicotinic acid	88	48	60	65
Thiamine (control period)	668	454	529	400
Thiamine (load test)	422	152	203	300
Riboflavin (control period)	810	387	399	400
Riboflavin (load test)	3,333	2,127	2,375	2,200
Pyridoxine	7	5	6·5	4·7

* Vitamin A—International Units per 100 ml. of plasma.
Carotene—International Units per 100 ml. of plasma.
Vitamin C—Mg. per 100 ml. of plasma.
Nicotinic acid—Urinary excretion in mg. in 14 hours after 500 mg. oral test dose.
Thiamine: Control period—Urinary excretion in gamma in 24 hours.
Load test—Urinary excretion in gamma in 24 hours after 1 mg. intramuscularly.
Riboflavin: Control period—Urinary excretion in gamma in 24 hours.
Load test—Urinary excretion in gamma in 24 hours after 5 mg. orally.
Pyridoxine—Urinary excretion in mg. in 4 hours after 50 mg. orally.

[Although isolated manifestations of vitamin deficiency in pernicious anaemia may respond to appropriate vitamin therapy, recent work has provided scant support for the view that cases of megaloblastic anaemia refractory to parenteral liver extracts are likely to show any marked general or haematological response to adjuvant therapy with any of the purified vitamins mentioned in this paper.] *L. J. Davis*

1864. **Pseudohemophilia. Case Study**
W. PERKINS. *Blood* [*Blood*] **1**, 497–503, Nov., 1946. 3 figs., 6 refs.

A case of haemorrhagic diathesis occurring in a 20-year-old white American male is described. The only persistent abnormality found was a prolongation of the bleeding time. The patient had been admitted to hospital because of bleeding into the knee-joint. He had been a " bleeder " from 1 year of age, and since childhood had been admitted to hospital 8 to 10 times because of uncontrollable bleeding. He was the fifth of a direct line of males to be a " bleeder ". The occurrence of the same " bleeding " condition in the patient's half-brother by his father's second wife was also a point of interest. The majority of the bleeding times varied between 7 and 40 minutes; the clotting time (Lee and White) lay between 5 and 10 minutes. Clot retraction was normal, and repeated blood counts showed the formed elements of the blood to be present in normal numbers. The platelet count was 300,000 per c.mm. The capillary fragility test was normal, as was also the prothrombin index. Plasma fibrinogen was 0·32 g.%. Hypocalcaemia (7·36 mg. per 100 ml.) was found on admission, when there was clinical evidence of tetany. A history of several previous attacks was also given. A failure of normal capillary constriction following trauma was demonstrated in the nail-bed, which finding the author believes to confirm the observations of Macfarlane.

R. Winston Evans

1865. **Pseudohemophilia**
S. ESTREN, L. SANCHEZ MÉDAL, and W. DAMESHEK. *Blood* [*Blood*] **1**, 504–533, Nov., 1946. 67 refs.

In most instances the haemorrhagic disorders can be classified as those associated with (1) deficiency in platelets—thrombocytopenic purpura; (2) a disturbance of the coagulation factors—haemophilia, hypoprothrombinaemia, fibrinopenia; and (3) a disturbance of the capillary wall—vascular or non-thrombocytopenic purpura. In some cases, however, the attempt to classify an instance of excessive bleeding becomes difficult. This paper deals with 11 such cases, which were characterized by an increased bleeding time in the presence of a normal coagulation time, normal platelet count, normal serum fibrinogen, a normal prothrombin time, and a normal clot retraction. An analysis of the literature since 1900 and of the routine tests used in the study of the haemorrhagic diatheses is given, together with a critical review of 62 similar cases reported. The cases selected from the literature and classified under the heading of pseudo-haemophilia were those which were considered to have been adequately studied and in which (*a*) there was a tendency to excessive bleeding; (*b*) at least one determination each of bleeding time, coagulation time, and platelet count had been made, and an adequate clinical history taken; (*c*) there was an increased bleeding time in the presence of normal blood platelets and a normal coagulation time. A positive family history of bleeding was recorded in 57 cases taken from the literature. In their own 11 cases the authors obtained a definite history of familial bleeding in 4 instances, and a questionable family history was elicited in one other. They conclude that sporadic cases of bleeding are fairly common, and that therefore the diagnosis of pseudo-haemophilia must be made in many cases regardless of a negative family history. Of the 62 cases from the literature, 33 were females and 29 were males. Of their own 11 cases, 7 were females and 4 males. There is thus a slight predominance of women (54·8% of the total series), but this is not considered to be statistically significant.

Of the total of 73 cases the sites of bleeding were recorded in 64 instances. Epistaxis was the most prominent symptom, occurring in 75% of the cases. The bleeding was usually spontaneous, and most intense during childhood; it became less frequent and less severe in adult life. Bleeding into the skin occurred in 70·3% of the total number of cases, and in over one-half of their own group. This symptom was manifested as easy bruising and spontaneous ecchymoses. Petechiae were rare. Bleeding from the gums was frequent, occurring in 39·1% of the entire group; dental extraction caused excessive bleeding in each of their 11 cases, and in 5 it was the immediate cause for investigation. Bleeding into the joints was recorded in 8 cases in the literature. Uterine haemorrhage occurred in 20 (76·9%) of the 26 women above the age of 12 years. The bleeding time was always increased. It varied from " normal " to over 300 minutes in the recorded cases, and from 2½ to

90 minutes in their own cases. It was often extremely variable, being greatly prolonged at one time, and only slightly increased or even normal at others. As there was some indication that the Ivy bleeding-time determination might show abnormalities when the Duke bleeding time was normal, and vice versa, both procedures were carried out; prolongation of either or both was taken to be abnormal. Of the 62 cases in the literature 53 (85·5%) had normal coagulation times. In their own group 8 of the 11 cases had values which were normal on some occasions and border-line or abnormal on others. In the other 3 cases coagulation time was normal. Of 54 cases in which the results of a capillary fragility test were reported, 23 (42·6%) showed increased fragility and 26 (48·1%) normal fragility, and in 5 cases the fragility was normal on some occasions. In their 11 cases the authors found 4 to show increased fragility.

The differential diagnosis of these cases from other types of haemorrhagic disease and the need for their recognition, particularly from the prophylactic standpoint, are stressed. Except for easily accessible local bleeding, therapy is at present ineffectual. The authors conclude that the cases which have been designated as pseudo-haemophilia probably represent a particular anomaly of the capillaries in which capillary retractility following trauma may be inherently defective. An appendix is given in which standard methods for the performance of haematological tests required in the investigation of a haemorrhagic disorder are explained and criticized. It is stressed that the Lee and White method for estimating the coagulation time may give normal values as high as 20 minutes or more.

R. Winston Evans

1866. **Nitrogen Mustard Therapy. Studies on the Effect of Methyl-*bis* (Betachloroethyl) Amine Hydrochloride on Neoplastic Diseases and Allied Disorders of the Hemopoietic System**

L. O. JACOBSON, C. L. SPURR, E. S. G. BARRON, T. SMITH, C. LUSHBAUGH, and G. F. DICK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 263–271, Oct. 5, 1946. 5 figs., 6 refs.

These authors have employed nitrogen mustard—methyl-*bis* (β-chloro-ethyl)-amine hydrochloride—in the treatment of leukaemia, Hodgkin's disease, and related disorders. Doses of 0·1 mg. per kilo of body weight have been used in courses of 1 to 7 daily injections; experience has shown that the most suitable course is one of 4 consecutive daily injections. In aqueous solution the drug undergoes a series of transformations, so that injections must be given within 5 minutes of the preparation of the solution. The required quantity is injected through the rubber tubing of a rapidly running intravenous saline drip. This method avoids the risk of local thrombophlebitis.

In most patients nausea and vomiting follow the injection in about 3 hours, and during the 4 days of the course anorexia is common. Changes in the blood can be observed within 6 days of the initial injection and reach a maximum during the second or third week. These changes are: a small drop in the haemoglobin level and erythrocyte count; a fall in the platelet count, usually to about 60,000 per c.mm., but at times to 20,000 per c.mm.; and a leucopenia, affecting first the lymphocytes and later the neutrophils. The total leucocyte count fell in one instance to 800 per c.mm., but in all cases return to normal levels occurred within 2 weeks of the lowest figures being reached. Transient purpura was seen in 4 of 59 cases, and infection—a recurrence of facial erysipelas—in one. There were no fatalities which could be attributed to treatment.

Twenty-seven cases of Hodgkin's disease were treated, and in all but two a remission varying in duration from 1 to 7 months was obtained. In 4 cases which had ceased to respond to irradiation, significant remission was obtained with nitrogen mustard. In 4 out of 6 cases of lymphosarcoma there were remissions of 3 to 18 months. In chronic lymphatic leukaemia an initial response occurred in all of 8 patients. Cases of acute leukaemia showed no improvement, and the results with chronic myeloid leukaemia were unsatisfactory. No change was seen in 2 cases of myelomatosis, and only transient improvement in 2 of sympathicoblastoma. In polycythaemia vera remission of symptoms and return of the blood count to normal levels occurred in all of 5 patients treated; improvement has been maintained for over a year in some cases. The authors conclude that the most encouraging results are those in cases of Hodgkin's disease which have become resistant to radiotherapy.

R. Bodley Scott

1867. **Megakaryocytic Reaction Localized in the Bone Marrow. Report of a New Hematologic Syndrome with Observations on the Origin and Development of Megakaryocytes and on the Derivation of Platelets**

V. DE LA FUENTE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 387–404, Oct., 1946. 5 figs., 15 refs.

In only two diseases, thrombopenic purpura and chronic aleukaemic myelosis, is the megakaryocyte the dominant feature of the pathological picture. Only one other case of acute megakaryoblastic leukaemia has been reported (von Boros, *Z. klin. Med.*, 1931, **118**, 697), and that is doubtful. In a Filipino housewife [no age is given], after an undiagnosed pyrexial illness, the present author found a bone-marrow reaction not previously recorded. In this there was a myeloid, erythroid, and, predominantly, a megakaryocytic hyperplasia. Clinically there was a microcytic hypochromic anaemia, unrelieved by massive doses of iron. He presents a detailed study of the various cells found—their character, origin, and development—and discusses the function of the megakaryocyte in the formation of platelets.

[The author's views are highly speculative.]

Henry Cohen

1868. **X-ray Therapy of Lymphogranulomatosis.** (Zur Strahlentherapie der Lymphogranulomatose)

W. DIEKER. *Strahlentherapie* [*Strahlentherapie*] **76**, 86–107, 1946. 99 refs.

1869. **Folic Acid in the Treatment of Pernicious Anemia**

L. M. MEYER. *Blood* [*Blood*] **2**, 50–62, Jan., 1947. 4 figs., 30 refs.

Respiratory Disorders

1870. **Penicillin in the Treatment of Bronchiectasis**
H. B. HARWOOD. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 809–814, Dec. 7, 1946. 5 figs., 12 refs.

The author reviews the effects of penicillin therapy in 20 cases of bronchiectasis, 14 of which were advanced and bilateral saccular types. The course of treatment lasted 3 weeks, and comprised injections of 15,000 units for adults and 10,000 units for children every 3 hours, daily intrabronchial instillations (by means of a laryngeal syringe through the cords) of 10,000 units for adults and 5,000 units for children, and weekly bronchoscopic lavage. Infections of the upper respiratory tract (especially of sinuses and antra) were dealt with before penicillin treatment was instituted, and during treatment postural drainage and inhalations were continued. Fifteen of the patients improved after the course of penicillin treatment; 4 remained stationary, after initial but temporary benefit; 1 died of bronchopneumonia complicated by a previously unrecognized tuberculosis. The author takes a guarded view. He points out that the bronchial deformities and disturbances of bronchial function which characterize these advanced cases are permanent and irreversible, and also that in the varied flora of these cases, details of which he tabulates both before and after treatment, some organisms are penicillin-resistant. Moreover, the duration of improvement is still unknown; only an adequate follow-up can show this. *Henry Cohen*

1871. **Hemolytic Streptococcic and Nonstreptococcic Diseases of the Respiratory Tract. A Comparative Clinical Study**
L. A. RANTZ, P. J. BOISVERT, and W. W. SPINK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 369–386, Oct., 1946. 17 refs.

In an earlier paper the authors claim to have shown that rheumatic fever is invariably preceded by a haemolytic streptococcus infection of the respiratory tract. They recall: (1) Lancefield's work on haemolytic streptococcus A strains, which are responsible for 90% of all streptococcal infections in certain areas; (2) that in the armed Forces only 25% of young adults infected with scarlatinogenic strains developed a rash; and (3) the work of Bloomfield and his associates who have pointed out that ordinarily the clinical manifestation of streptococcal infection of the respiratory tract is an exudative tonsillitis and that tonsillectomy confers a high degree of immunity against such infection. Bloomfield's series was small, and as doubt has been cast on his conclusions the authors have reviewed the condition and present in this paper an analysis of the clinical and laboratory data from a larger number of respiratory tract infections occurring in military personnel; these data in general confirm Bloomfield's findings.

The troops examined were well seasoned and thus more comparable to a civilian population than would be new recruits, who are highly susceptible to respiratory infections. All patients with acute respiratory infections were admitted to hospital, but all examples of common communicable disease, Vincent's infection, and pneumonia are excluded from this report. The history and physical signs were recorded, cultures were made from nose and throat when the patient was admitted, and later repeated, and all isolated haemolytic streptococci were classified serologically into groups and types by means of the precipitin techniques of Lancefield. In addition, leucocyte counts and erythrocyte sedimentation rates were determined, and an immunological study was made which included measurement of the antistreptolysin and antifibrolysin titre of serum and plasma on the second, ninth, and twenty-first day of the illness. [Detailed results of these are not included in this paper.]

The cases reported include 871 of non-streptococcal infection, 93 of Group A carriers, 342 of haemolytic streptococcal infections (300 with antibody response, and 42 without), and 27 scarlet fever patients. The following table [compiled by the abstracter] summarizes the significant differences found by the authors between haemolytic streptococcal and non-streptococcal infections, though in 10% of cases the latter simulate the former.

	Haemolytic Streptococcal Infection	Non-streptococcal Infection
Febrile symptoms (headache, aching, chills, prostration)	Usually observed	Usually observed
Sore throat	Severe	Minimal
Dysphagia	92%	34%
Cough, severe ..	2·3%	24·1%
Hoarseness	1%	13·1%
Laryngeal tenderness	Rare	Common
Tonsillar and pharyngeal exudate	Large: 44% Small: 18·3%	Absent: 95%
Oedema — tonsils, fauces, soft palate, uvula	Marked in 85·7% (often without exudate)	Absent or minimal in 89·1%
Abnormal redness of these areas	Extreme in 83·6%	Absent or minimal in 76·2%
Tenderness of cervical nodes	80·9% (43·6% very severe)	13·6% (1·7% very severe)
Leucocytosis ..	49·1% over 13,000	Very rarely over 13,000
E.S.R.	70·8% — over 20 mm. in 1st hour	Usually less rapid

The absence of tonsils did not affect symptoms, but the local throat signs were less severe, which made the diagnosis more difficult. A scarlatiniform rash was observed in 27 persons; the findings in them were

essentially similar to those in streptococcal infections without a rash. Even without bacteriological study the typical pictures of the two groups can be recognized with only 10% of error. Group A haemolytic streptococci were present in the throats of from 5 to 20% of the healthy camp population. The error in the published data which results from this carrier rate, such as from the finding of haemolytic streptococci in the throats of non-streptococcal cases is, if both clinical and laboratory studies be considered, only 1 to 2%. Haemolytic streptococci of groups C and G account for about one third of the 5% of haemolytic streptococcal infections not due to Group A.

[This excellent study is written in so terse a style that its further condensation is difficult. The authors do not refer to the therapeutic tests with sulphonamides and penicillin, possibly because of obvious fallacies. They promise to report their laboratory investigations in detail later, but they note that a rising antistreptococcal titre is often absent in haemolytic streptococcal infections.] *Henry Cohen*

1872. **Haemoptysis and Bronchoscopy. Statistics of 80 Cases.** (Hémoptysies et endoscopie bronchique. Une statistique de 80 cas.
P. MOUNIER-KUHN, C. OLLAGNIER, and A. PERSILLON. *Poumon* [*Poumon*] **2**, 193–203, July–Aug., 1946. 5 refs.

The authors put forward a plea that bronchoscopy should not be considered as a diagnostic agent to be used only as a last resort, but that it should be employed in every case of haemoptysis for which there is not an adequate explanation. They review 80 cases in which bronchoscopy was carried out, and conclude that in more than 90% the origin of the bleeding was ascertained and the exact site and aetiology of the lesion were confirmed. In addition, in a number of the cases, bronchoscopy was the means of correcting an erroneous diagnosis. It is pointed out that it was only in 1930 that a tracheobronchitic origin of the bleeding was suggested, and that for some time afterwards pulmonary bleeding was considered to be for the most part tuberculous and tracheobronchitic bleeding non-tuberculous.

The cases are divided into 6 groups: (1) Due to haemorrhage from the trachea. This group is the largest (47·5%), the condition being more prevalent in women of 20 to 40 years of age. Of the 38 cases 11 had diffuse congestive lesions, bleeding freely on contact, and 27 were localized. Nineteen lesions were tuberculous, 1 was hypertensive, 2 were due to external causes, and the 16 others to diverse causes. (2) Due to bronchial tumours (17·5%). Most of the patients were over 50 years of age. There were 18 " epitheliomata " but only 10 of the patients had had a haemoptysis, and only 5 of these had bleeding to any marked degree. There were 4 cases of benign tumours, 3 of which had been previously treated as cases of tuberculosis, 1 with a pneumothorax. (3) Due to dilatation of the bronchus (15%). The ages of the patients varied from 20 to 45. Four were cases of bronchiectasis showing classical symptoms of the condition, and 8 had haemorrhage alone as a presenting symptom. (4) Due to stenosis of the bronchus (7·5%). Three of these were tuberculous, but the authors point out that in their experience haemorrhage in such cases is rare. Two were syphilitic and 1 was due to chronic inflammation. (5) Due to various causes (5%). Four cases fell into this group—" bronchial stone ", rupture of a gland through the bronchial wall, a Boeck's sarcoid, and a case of bronchospirochaetosis. (6) Those cases (6) in which there were negative results (7·5%). No haemorrhagic area or any indication of the cause of the bleeding could be found. *Richard D. Tonkin*

1873. **Clinical Aspects of Haemorrhagic Tracheitis.** (Quelques aspects cliniques de la trachéite hémorragique)
—. LAGEZE, P. MOUNIER-KUHN, —. CAHEN, and C. OLLAGNIER. *Journal de Médicine de Lyon* [*J. Méd. Lyon*] **27**, 681–688, Oct. 5, 1946.

Five cases are described in which repeated haemoptysis was ascribed after bronchoscopic examination to a haemorrhagic tracheobronchitis. The mucosa of the trachea was thickened and congested on one face of the carina and similar changes were observed in the main bronchus; dilated small vessels which bled easily were seen when the thickening had subsided. In one case partially calcified mediastinal nodes were seen on tomography, and the condition was considered to be secondary to these. In another there was an old tuberculous lesion in the left upper lobe which was regarded as healed.

[The responsibility of the tracheobronchial lesions for the haemoptyses in these cases does not appear established, and bronchography was not carried out. No evidence of a relationship to tuberculosis of mediastinal lymph nodes is brought forward.] *J. W. Litchfield*

1874. **The Activity of Penicillin in the Intranasal Pneumococcus Infection of Mice**
M. BUCK, N. ERCOLI, D. R. KELLY, M. N. LEWIS, and R. J. SCHNITZER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 306–311, Sept., 1946. 16 refs.

The authors have studied the effect of penicillin in controlling pneumococcal infection in mice after intranasal inoculation. Mice were exposed for 2 minutes to ether vapour, then their noses were dipped in cultures of pneumococci. Untreated mice died within 30 to 48 hours with pneumonia and septicaemia. Previous experience had shown that sulphonamides, which were effective against pneumococci injected intraperitoneally into mice, were only exceptionally effective against the intranasal infection. Nevertheless a total of 800 to 1,000 units (per mouse of 20 g.) of sodium penicillin given subcutaneously reduced the death rate to 50% or less in the case of type I pneumococcal infection; a larger minimal dose (about 1,800 to 2,000 units) was necessary in type II infections. In type I infections penicillin was given either as a single treatment 1 hour after inoculation, or in two, three, or four divided doses. In type II infections repeated doses only were given. The effect of two or more doses was investigated. Lung cultures were made 1, 3, 5, 9, and 25 hours after intranasal inoculation and a single treatment with 1,000 units

of penicillin. Pneumococci diminished gradually at first and were very scanty at 9 hours, but at 25 hours there was again a profuse growth. When a second treatment with 1,000 units was given 4 hours after the first the lungs were sterile at 9 hours and again at 24 hours. In type II infections the minimal effective dose of penicillin was 2,000 units whether the drug was administered orally or subcutaneously. The penicillin concentration in the sera of mice was estimated at intervals after the subcutaneous and oral administration of varying doses. The peak of the concentration after subcutaneous injection in all dosages was at least 10 to 20 times higher than the maximum noted after oral administration, but the concentration dropped rapidly. Oral administration gave a more consistent serum level which persisted longer. In the prophylaxis of type II infections doses of 2,500 and 5,000 units were also equally effective whether they were administered subcutaneously or orally. Penicillin was given either immediately, or 1, 3, or 5 hours before intranasal inoculation.

The authors suggest that in the prophylaxis and treatment of infections which require large doses of penicillin high peak concentrations have little influence, but that the sustained lower concentrations in the blood are alone effective. Thus for an equal effect the same dose may be given subcutaneously or orally. There are not sufficient data for applying these findings to treatment of human beings, though there is some evidence that adequate doses by mouth may be useful in conditions in which it is necessary to maintain a consistent blood level over a comparatively long time. *D. G. ff. Edward*

1875. **Pulmonary Mycosis**

T. G. BROWN. *Edinburgh Medical Journal* [*Edinb. med. J.*] **53**, 583–586, Oct., 1946. 2 refs.

Laboratory observations made during the past few years seem to the author to indicate that mycotic disease of the lung may be more common in this country than is generally suspected. Among sputa examined for tubercle bacilli he found a number of specimens which looked like watered milk. Generally they were fluid and of a greyish-white colour. After the specimen had been standing a dead white flocculent deposit separated rapidly from a slightly opalescent supernatant fluid. Microscopical examination showed that the deposit was composed of epithelial cells and macrophages with either very few or an entire absence of polymorphonuclear and lymphocytic cells unless the sputum was infected with secondary organisms. This appearance of the sputum was " unlike any reactive result of the usual bacterial infections " and suggested a proliferative rather than an inflammatory process. Spores of varying sizes, usually oval and doubly refractile, might be demonstrated, though this was not a constant finding. Culture on Sabouraud's medium invariably gave a growth typical of *Candida albicans*.

During 12 months specimens of sputa having this characteristic appearance were examined from 467 persons. *Candida albicans* was isolated in all cases and the fungus was invariably found on subsequent examination during the next few months. Sputa from 59 persons contained tubercule bacilli as well as the fungus. Eight brief case histories are presented. Two cases of familial infection are cited, but it is pointed out earlier in the article that mycotic infection is believed to take place, not from case to case, but by inhalation of spores present in dust. Two sisters were in a sanatorium without confirmatory bacteriological evidence of tuberculosis, while their brother at home was under observation. All three had typical mycotic sputa from which *Candida albicans* was isolated repeatedly and all attempts to prove a tuberculous basis for their illnesses proved sterile.

[This paper is a stimulating, if very brief, introduction to the subject. The abstracter has had the opportunity of examining these sputa, macroscopically, microscopically, and by culture methods, and has been shown the lethal effects of inoculating rabbits with the organism. The laboratory work is impressive. The vital question of human pathogenicity of the organism, however, is not discussed in this article, the case summaries are inadequate, and the author does not describe radiological appearances, clinical signs, or response to treatment. True bronchopulmonary moniliasis is said to respond readily to massive dosage with potassium iodide and to intravenous gentian violet. For the single species, *C. albicans*, no less than 172 synonyms exist in the literature, the most familiar of these being *Monilia albicans* and *Oidium albicans*. This yeast can be isolated frequently from the stools, vagina, skin, and throats of apparently healthy individuals, and may be found in sputa from patients with tuberculosis, lung abscess, and other pulmonary conditions. Castellani showed that the fungus might occur in sputum as: (1) a non-virulent organism; (2) a secondary invader, which, though lethal on intravenous inoculation into a rabbit, did not cause disease on inhalation; and (3) the causal factor of disease, proved by inoculation. It is clear that further clinical, radiological, therapeutic, and (if possible) human histological studies are urgently called for if we are to exclude a " red herring " and establish the finding of a new disease in this country.] *T. Semple*

1876. **Pneumoconiosis in South Wales Anthracite Miners**

C. G. GOODING. *Lancet* [*Lancet*] **2**, 891–896, Dec. 21, 1946. 15 refs.

This review of coal-miners' silicosis is based on clinical experience and pathological findings. Gradually increasing dyspnoea is the outstanding symptom and this is often made worse in later life by cardio-renal failure. Cough is frequently absent or unproductive in uncomplicated cases; persistent or recurring black sputum indicates that the lung lesions are breaking down. Even in advanced stages of the disease symptoms may be few or entirely absent and, when severe, indicate added infection. Physical signs are surprisingly slight and those of diminished air entry predominate even with advanced lesions. At necropsy widespread adhesions and thickened pleurae are seen with gross emphysema, while spontaneous pneumothorax from rupture of a bulla is an occasional complication. The cut surface

of the lung presents a variable picture from that of classical silicosis (discrete nodules without blackening) seen in rock-workers who have been consistently exposed to dust with a high content of pure silica to a massive type of fibrosis (like solid black rubber) seen in the lungs of workers at the coal face. These massive consolidations may crumble and disintegrate, and are often extensively excavated and filled with semi-liquid inky material, which provides the black sputum of silicotic coal miners. Tracheo-bronchial lymph nodes are usually enlarged, black, and fibrotic.

In coal miners tuberculosis is atypical and difficult to recognize; even in sputum-positive individuals it may not be obvious at necropsy, and in the more common sputum-negative cases it is not easy to decide how much of the disintegration and cavitation is due to tuberculous infection. Silica is an adjuvant to tuberculosis: coal dust is credited with an inhibitory effect; and interplay of these two is probably responsible for much of the modification of tuberculosis seen in silicotic coal miners. The average survival period of 53 men certified as having silicosis with tuberculosis was only 22 months. In the author's series of 227 necropsies on certified silicotics it was found that 59 (26%) had associated tuberculosis and 41 (18%) had non-tuberculous respiratory affections; 84 (37%) had died from cardiac failure and 43 (19%) from unrelated conditions. Non-tuberculous infection usually takes the form of bronchopneumonia; by reducing the available reserve of functioning lung tissue pneumonoconiosis impairs the chance of recovery from a pneumonia. Cardiac embarrassment, usually right-sided, is a common sequel or concomitant, especially in men with massive lesions. Only one case of primary lung cancer could be found in records of 400 necropsies. Preventive measures include water spraying, wet drilling, and the provision of an ample ventilating current to dilute and remove such fine dust as escapes the water traps. Hard headings are now considered safer than the coal face, where it is much more difficult to suppress dust, which is fortunately less harmful here.

Although the amendment of legislation in 1943 has done much to prevent the march of silicosis no person has the power at present to keep the tuberculous man out of the pit, and until this state of affairs is altered routine medical and radiological examinations can do little to prevent spread of the infection. *T. Semple*

1877. Spreading Suppurative Pneumonitis

T. H. Sellors, L. G. Blair, L. E. Houghton, V. C. Thompson, and D. M. Pryce. *Thorax* [*Thorax*] **1**, 146–181, Sept., 1946. 45 figs., 21 refs.

There has been increasing recognition during the past few years of the occurrence of pulmonary cavitation consequent upon non-specific inflammatory processes. The authors present a study of this condition, which they designate " spreading suppurative pneumonitis ", based upon 27 cases admitted to Harefield Thoracic Surgical Unit over a period of 5 years. These cases all showed spreading pneumonitic changes, associated with cavity formation and a productive cough with purulent sputum, and in none was any specific organism found to be responsible, or even predominating.

Radiographs in the early stages revealed an homogeneous opacity of the lung, suggestive of irregular massive consolidation, and, later, evidence of softening, but not at such an early stage as in an acute putrid lung abscess. The subsequent behaviour of the lesions was diagnostic, and the essential feature was direct extension of the consolidation to areas immediately adjoining, with partial resolution of the area first involved—that is, a creeping spread, uninfluenced by interlobar planes. In most cases the whole lung was at some time involved, but an extension to the opposite side was rare and occurred in only one instance as a terminal event. When the active stage of the disease subsided, fibrosis and bronchiectasis resulted in considerable lung damage.

The variability of the picture and unpredictable nature of the course of this condition are emphasized, but there are enough constant features to permit a standard description. The average age of the patients was 46·5 years, and 25 of the 27 were males. The patients complained of the sudden onset of severe cough and copious sputum, often accompanied by sweating, prostration, and pain in the chest. In half the cases there was a prodromal illness suggestive of a " cold " or mild attack of influenza. In others the condition followed a dental extraction or severe exposure. Haemoptysis was a fairly frequent feature. A moderate degree of fever was present. The physical signs were those of a bronchopneumonia, but in some cases there were extensive areas of consolidation. The sputum soon became purulent; in three-quarters of the cases it was foetid at some stage of the disease, if not at the onset. There was a low-grade leucocytosis, the maximum being 17,000 cells per c.mm. Remissions and relapses occurred during a period of months rather than of days. Toxaemia in the acute phases was severe and resulted in death in 6 cases. Empyema did not occur, but there were 2 cases of cerebral abscess, 1 being post-operative.

At necropsy, the lungs showed extensive adhesions, thickening of the septa, areas of emphysema, collapse and pneumonitis, multiple abscess cavities, and enlargement of the lymph nodes. Some of the more acute cavities contained a slough, attached proximally where the necrotic bronchi entered, while others had a fibrous wall and were lined with columnar or even squamous epithelium. The cavities originated in the breakdown of pneumonitic lung and spread by ulceration. The possibility that the squamous metaplasia of the respiratory epithelium results from a local vitamin-A deficiency is mentioned. The aetiological agent is not known.

The literature of pulmonary suppuration as a whole is reviewed. It is pointed out that the cases described do not completely coincide with those recorded by other writers but there is much in common. The following suggested classification of lung abscess is given. Cavities may develop as a result of (1) a pneumonic process, (2) bronchial obstruction, or (3) vascular embolism. (1) The pneumonic form is subdivided into (*a*) specific forms—for example, tuberculous or staphylococcal—and (*b*) non-specific forms, spreading suppurative pneumonitis being an example. (2) The form consequent upon

bronchial obstruction may be sub-lobar—peripheral acute putrid lung abcess, occasioned by the inhalation of infected matter—or it may be lobar (usually multiple) and occur as the result of lobar collapse. (3) Embolic forms arise from infection carried from other parts of the body and may be single or multiple.

The condition may be confused with obstructive and embolic lung abscess, pulmonary tuberculosis and neoplasm, or, less commonly, with bronchiectasis with added pneumonitis, infected cysts, actinomycosis, or adenomatosis of the lung. The outlook is not good, and at best the patient is faced with a long illness. The average duration of symptoms before admission to the chest unit was 8½ months. There is prospect of cure by conservative measures in less than 20%, and if the condition has existed for more than 2 months the prospect is even worse. Of the 27 patients in this series, 10 died, 8 improved, and in 9 the condition resolved, 5 with conservative treatment only and 4 following pulmonary resection.

The prime need in treatment is rest in bed, especially during the acute and febrile stage. Diet must be liberal and tempting and protein intake generous, particularly if the sputum is copious. Anaemia is controlled by iron, and, if necessary, by blood transfusion. Results with sulphonamides were disappointing, and all cases relapsed as soon as the drug was withdrawn. Penicillin was slightly more effective but again there was relapse on withdrawal. Bronchoscopy as a therapeutic measure had little value. Physiotherapy was of great help during the whole course of the illness; in the acute stages it should be confined to postural drainage. In this series drainage operations were consistently failures, and the authors consider that an artificial pneumothorax is dangerous in the acute stages and impracticable in the chronic. Pneumonectomy and lobectomy are the only procedures which will save the lives of certain patients. Owing to the tendency of the disease to spread across the fissures, it is necessary in most cases to remove the whole lung. The procedure is severe, and in the present series there were 3 deaths out of 7 operations. There are two distinctive stages at which operation is indicated: (*a*) during the acute stage, to check a progressive deterioration, and (*b*) in the late phase when the patient is left with a bronchiectatic and cavitated lung. In the first instance the surgeon has to contend with severe toxaemia, and in the second with an operation of great technical difficulty. The article is illustrated by 6 detailed case histories. *Richard D. Tonkin*

1878. **Cystic Emphysema.** (L'emphysème kystique. (Etude anatomoclinique—A propos de huit observations)) —. PALIARD, —. PLAUCHU, —. GALY, and —. PAPILLON. *Poumon* [*Poumon*] **2**, 205–235, July–Aug., 1946. 25 figs., 84 refs.

After a brief historical outline the authors present their survey of cystic emphysema under three headings: pathological anatomy, aetiology, and clinical study. In the section headed pathological anatomy they divide emphysematous bullae into two groups according to their site. Alveolar bullae are present in the pulmonary parenchyma, and interstitial bullae, less well known, are seen in an interlobar or subpleural situation. The alveolar type is sub-divided into: (1) Giant emphysematous bullae found post mortem in emphysematous patients. The bullae are peripheral and balloon the surface of the lung; they are often multiple and of various sizes. They begin as simple exaggerations of the emphysema, but later only a skeleton of alveolar parenchyma remains. No cellular envelope is seen and the structure is homogenous. They correspond to a state of atrophic destruction. (2) Sclero-atrophic emphysematous bullae found at the edge of an area of dense sclerosis. Histologically they are the same as the giant bullae but they have a fibrous-tissue base. (3) Obstructive emphysematous bullae, which differ only in being near a bronchus obstructed by a tumour or foreign body. (4) A special form of broncho-alveolar cyst seen in the *maladie de Bourneville* and disseminated throughout a congested lung.

A congenital origin for the bullae is considered to be rare, though some subpleural bullae seem to develop from malformed pulmonary tissue. The majority are acquired. Alveolar emphysematous bullae develop out of a simple atrophic emphysema, which is a disease of the alveolar wall. It may be associated with asthma and other pulmonary infections, or may be of cardiac origin. Two mechanical causes have been suggested—a valvular and a rupture of the alveolar walls. The authors draw attention to the regressive type of emphysematous bullae, and declare that the pathological structure is unknown and is unlikely to be the same as that described above.

In the clinical study the authors divide bullae into emphysematous bullae seen in the sclerotic emphysematous lung and transitory bullae seen in the lungs of children during bronchopneumonic affections. The first are discovered radiologically, are large, and show no surrounding congestion. Displacement of heart shadow and mediastinal hernia may be present. The outlines are difficult to define because of the emphysema. Post mortem the bullae are seen to be acompanied by smaller bullae of similar structure. The symptoms are dyspnoea and haemoptysis. Clinically there may be disappearance of the cardiac dullness, with displacement of the heart. The outcome is one of progressive respiratory insufficiency. Some patients may become secondarily infected, some may die from cardiac involvement. In the transitory type seen in children round shadows may be apparent in the radiograph. Their anatomical interpretation is unknown since few cases come to necropsy. They appear during the resolution of pneumonic processes and in the course of bronchial infections and infectious diseases. The bullae are usually single and may grow to a large size; they occasionally contain fluid. They can retrogress and may entirely disappear.

Diagnostically the condition of cystic emphysema must be differentiated from tuberculosis with cavity formation, spontaneous pneumothorax, and bronchial cysts. The history and radiological characteristics may indicate the diagnosis, but bronchography and thoracoscopy may be necessary. Treatment in most

cases must be directed to the underlying illness. Complications, however, may need specific treatment. Recurring spontaneous pneumothorax may necessitate obliteration of the pleural space by injection of blood. Surgical resection by thoracotomy has been carried out for a cortical emphysematous bulla, and puncture of a cyst with aspiration of the air has been useful in cases of acute progressive dyspnoea. *Richard D. Tonkin*

1879. **Primary Atypical Pneumonia with a Report of Sixty Cases**
D. W. CHAPMAN. *Texas State Journal of Medicine* [*Tex. St. J. Med.*] **42**, 362–366, Oct., 1946. 21 refs.

This account of primary atypical pneumonia is based on a survey of part of the literature and on an analysis of 60 civilian cases. No indication is given of whether the cases were sporadic or occurred in an epidemic. Of the group, 26 were in females (44%). The author, as is usual in the American literature, considers that primary atypical pneumonia is a nosological entity due to a filterable virus. There was no mortality in his series and the main complication seen was pleural effusion in 3 cases.

[He makes no new observations on the clinical, radiological or laboratory findings.] *Howard Nicholson*

1880. **Primary Atypical Pneumonia. A Disease of Segmental Distribution**
W. E. CRYSLER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **56**, 324–336, Sept., 1946. 19 figs., 9 refs.

This account is based on the *x*-ray appearances in approximately 1,000 cases of primary atypical pneumonia. The author points out that in established cases the consolidation is confined to the bronchopulmonary segment supplied by a secondary bronchus, the only exceptions noted being occasional cases in which the lesions were confined to a tertiary segment, usually one of the tertiary segments in the cone supplied by the ventral branch of the upper lobe bronchus. Eighty per cent. of infiltrations were seen in the lower lobe, the dorso-basilar segment being the most common site. The dorsal segments of the upper lobe were never involved, an important distinction from pulmonary tuberculosis.

The radiological appearances of consolidation of the secondary bronchopulmonary segments in postero-anterior and lateral projections are described and illustrated. Attention is called to the fact that left dorso-basilar consolidations may be completely concealed by the cardiac shadow in the postero-anterior film and are only revealed if lateral views are taken [a not infrequent cause of failure to diagnose atypical pneumonia]. The usual position of the apices of the lower lobes was found to be opposite the eighth costovertebral junction on the right and the sixth on the left; in one case it was shown that there was a difference of three interspaces between their positions in full inspiration and expiration. [This is considerably greater than that given in the standard anatomical description and appreciably greater than Brock found from thoracotomy, dissection, and radiological studies. In the case illustrated of the right apical segment of the lower lobe, the upper border is below the hilum and some degree of atelectasis may well have been present.]

The frequency of minimal atelectasis (20%) and the occasional occurrence of bronchiectasis (2%) and secondary infection, combined with the distribution of the lesions, suggest that the infection results from the aspiration of infected material. The developing infiltration appears as a peri-bronchial shadowing which becomes confluent, the process being reversed during resolution.

[This paper gives a refreshingly exact account of the radiological appearances of primary atypical pneumonia, and all cases seen by the abstracter in the Mediterranean region corresponded to the secondary segmental distribution. It is to be regretted that no detailed analysis of the cases is given. The author's nomenclature of the secondary and tertiary bronchi has been used but it is surely time that a standard terminology was decided on by an authoritative body.] *J. W. Litchfield*

1881. **Changes in Haemoglobin Concentration in the Acute Stage of Lobar Pneumonia**
M. S. FERGUSON. *British Medical Journal* [*Brit. med. J.*] **1**, 131–133, Jan. 25, 1947. 2 figs., 7 refs.

The pneumonic process must lead to a loss of plasma into the affected lung. Loss of protein from the plasma would cause a mechanical haemodilution, and in normal circumstances the normal levels would quickly be recovered, but in pneumonia the haemoglobin concentration continues to fall. The methods of investigation involved the study of heparinized venous blood taken from cases of pneumonia, which was used to estimate the plasma protein by a refractometric method, and the haemoglobin concentration by a photoelectric "Spekker" instrument. Some graphs accompanying the article show the progress of these estimations at intervals, starting from the time of the patients' admission to hospital.

The author points out that the low plasma protein and low haemoglobin levels found in pneumonia are not in themselves causative factors in delaying resolution, but the findings indicate an extensive and dense consolidation which is itself a prime factor in the speed with which resolution is concluded. The presence of low plasma protein concentration and low haemoglobin in cases of pneumonia does not cause delayed resolution, but merely parallels the density of the consolidation, which is itself important in deciding the time of resolution. *R. G. Bannerman*

1882. **Pneumothorax and Pulmonary Arterial Pressure.** (Neumotórax y presión pulmonar)
V. A. J. ALBERTI. *Anales de la Cátedra de Patologia y Clinica de la Tuberculosis* [*An. Cáted. Pat. Clin. Tuberc.*] **7**, 281–289, Dec., 1945. 3 figs., 52 refs.

1883. **On the Incipient Stages of Porcelain Silicosis.** [In English]
P. ESKILDSEN and P. G. MØLLER. *Acta Radiologica* [*Acta radiol., Stockh.*] **27**, 601–606, Dec. 20, 1946. 3 refs.

Digestive Disorders

1884. **Objective and Clinical Study of the Tongue. Comparison of Normal, Desquamated, and Atrophic Tongues by a Tongue Print Method**
J. R. DiPALMA. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 405–418, Oct., 1946. 9 figs., 4 refs.

Among the methods designed to secure permanent and analysable records of the surface pattern of the tongue are: (1) the use of smoked paper to make tongue prints, and (2) monochromatic or colour photography, both macro- and microscopical. The author describes an inking solution made by heating at boiling-point for 10 minutes in a water bath 2 g. of Evans blue, and 10 g. of gum acacia in 40 ml. of distilled water. A few drops of chloranobutanol is added on cooling to prevent the growth of moulds. This creamy solution is odourless, tasteless, and non-poisonous, and has excellent spreading and printing qualities (kymograph paper is suitable for printing); it dries rapidly and can be used for a permanent record. A little practice is necessary to secure prints which can be compared. Only the distal third of the tongue can conveniently be examined.

Using this method the author has studied the filiform and fungiform papillae, and the folds, fissures, and creases in the lingual mucous membrane, both qualitatively and quantitatively, in 99 normal, healthy male medical students. In a circle 0·5 cm. in diameter and 1 cm. from both the tip of the tongue and the mid-line, an average of 52·2 filiform papillae was found. Similar-sized circles for the enumeration of fungiform papillae were studied on the margins of the tongue, and contained 8·1 such papillae. Tongues varied and according to the dominant feature could be classified as: (1) filiform, (2) fungiform, (3) slightly fissured, (4) fissured, and (5) linear. The abnormal tongues studied were in 15 patients with definite dietary deficiencies and in 7 with pernicious anaemia. In these the filiform papillae were markedly decreased and the fungiform slightly increased. In addition the latter showed: (1) a cross-patched pattern, attributed to thinning of the lingual mucosa, which allowed the impression of the underlying lattice work of fibromuscular structures to print through, and (2) longitudinal ridging, due probably to shrinkage of the intrinsic muscles of the tongue throwing the mucous membrane into longitudinal folds, or possibly to hyperplastic mucosal changes. The tongue in pernicious anaemia is indistinguishable from that in dietary deficiency.

The author pleads for a rational classification of abnormal tongues based on the papillary pattern. He would recognize three groups only: (1) normal tongues, with papillae intact both in number and structure; (2) desquamated tongues, in which filiform papillae are decreased or absent, but fungiform papillae are intact; and (3) atrophic tongues, in which filiform papillae are absent and fungiform papillae much decreased.

Henry Cohen

1885. **The Effect of Dietary Carbohydrates on the Dental Flora of the Rat**
E. I. PARSONS, E. V. McCOLLUM, and M. FROBISHER. *American Journal of Hygiene* [*Amer. J. Hyg.*] **44**, 249–256, Sept., 1946. 4 figs., 6 refs.

An attempt was made to vary the bacterial flora of the teeth in rats by alteration in diet. The organisms were isolated from crypts and fissures of the teeth and not from the saliva, and cultivation was carried out both aerobically and anaerobically. The authors describe fully the bacteriological technique and the method of enumeration by proportionate logarithm tables. The rats used came from the McCollum colony of rats and careful controls were made at each stage of the experiment.

The types of bacteria found in any given subject remained constant, but there were striking variations in the ratios between the different organisms. Attention was paid chiefly to the presence of cocci (both acid-forming and non-acid forming) and lactobacilli. To the basic diets were added sucrose, lactose, raw starch, and cooked starch in 10, 20, 40, and 60% concentrations, and the flora found was compared with that in the teeth of rats maintained on a basic diet. The addition of 10% or more of any carbohydrate greatly increased the number of acidogenic cocci in the crypts. Lactose and raw starch favoured the growth of the lactobacilli, but these organisms were never found in numbers greater than a quarter of the others, and were usually much less numerous. Yeasts and strict anaerobes were not seen in significant numbers.

D. Robertson-Ritchie

1886. **Peptic Ulcer of the Esophagus. Report of a Patient with 10 Year Follow-up**
D. R. MORTON and A. BRUNSCHWIG. *Gastroenterology* [*Gastroenterology*] 7, 314–319, Sept., 1946. 3 figs., 8 refs.

A single case is reported of peptic ulcer of the oesophagus in a woman aged 65. In 1935 her condition was diagnosed radiologically as carcinoma of the oesophagus from the presence of a constricted rigid area extending for 10 cm. at the level of the seventh dorsal vertebra. The endoscopic appearance also suggested carcinoma but three successive biopsies showed only chronic granulation tissue without epithelium. A gastrostomy was done and the patient's health rapidly improved. A further barium swallow in 1937 revealed an almost occluded oesophagus, but the patient's general health was excellent. She was then lost sight of until 1945, when she returned to the clinic at the age of 75 with a history of 5 months' intermittent vomiting. The radiograph of the oesophagus was much the same as in 1935, but a 3 mm. duodenal ulcer crater was also found. A fractional histamine test meal was normal and so were the other laboratory findings. She was discharged in good condition after 3 weeks'

medical treatment for ulcer. The authors claim that the case proves how satisfactory the treatment of oesophageal ulceration can be without recourse to a gastrostomy.

[As seen in the reproductions of the radiographs, the "ulcer" was of an unusual type. The differential diagnosis of its aetiology (regurgitation of acid associated with a pyloric lesion, ectopic gastric mucosa, and hiatal hernia) is not discussed.] *Denys Jennings*

1887. **The Effect of Pilocarpine on Mucus Secretion by the Pyloric Mucosa**
J. S. IVY. *Gastroenterology* [*Gastroenterology*] **7**, 224–230, Aug., 1946. 20 refs.

A review of the literature on the effect of pilocarpine on mucus secretion by the pyloric mucosa showed that reports were inconsistent, and Hollander (*Gastroenterology*, 1944, **2**, 201) concluded "that there was considerable doubt whether pilocarpine exercises any direct mucus-stimulating action whatever". One of the problems appeared to be to eliminate the mechanical squeezing out of mucus from the cells due to the motility stimulated by the drug. To test the effect of this factor pyloric pouches, which were everted so that the mucosa did not rub against anything when the musculature contracted, were made in each of 3 dogs. No attempt was made to denervate the pouches. After from 3 to 5 weeks the mucus was collected by placing a large glass funnel over the pouch. Control collections were made for several hours, and then 5 mg., or approximately 0·4 mg. per kilo, of pilocarpine hydrochloride was injected subcutaneously. Specimens were collected every half-hour. The volume of the insoluble mucus was measured by centrifuging for 30 minutes. The base was titrated with 0·037 N hydrochloric acid, using Töpfer's indicator. Following the injection of pilocarpine the mucosa changed from a bright-red to a purplish-red colour, indicating that vascular changes were occurring. Movements on the surface of the mucosa were not noticed.

From the tables included it can be seen that, with no exceptions in the averages, there is a decrease in the total volume, total titratable base, and total reducing substances in mucus after the injection of pilocarpine. On the other hand, the average values for the volume of insoluble mucus showed an increase after the injection of pilocarpine. When the results are subjected to statistical analysis, however, there is no determination showing a statistically significant difference before and after the injection. The author concludes that pilocarpine does not stimulate the secretion of mucus by the pyloric mucosa of a dog when precautions are taken to prevent the rubbing together of the folds of the mucous membrane. *N. S. Plummer*

1888. **Vascular Changes in the Mucosa in Experimental Nutritional Gastritis**
B. N. BERG. *Gastroenterology* [*Gastroenterology*] **7**, 340–354, Sept., 1946. 12 figs., 18 refs.

The author makes the distinction, so important in human peptic ulcer, between lesions in the non-acid-producing antral mucosa and lesions in the fundal acid area. Albino rats 28 days old were fed for periods of 14, 28, and 56 days on a low-calcium diet to produce antral ulcers. Fundal lesions were produced in rats 40 days old by starvation for 2 to 4 days and in rats 28 days old by thiamine-deficient diets for 4 weeks. Rats on a stock diet were used as controls. At the end of the experimental period the right auricle was opened under ether narcosis and the rats were exsanguinated. A 20-gauge needle was inserted in the thoracic aorta and a 10% suspension of indian ink in 8% gelatine was injected until there was a free backflow through the auricle. The stomach was then removed, washed in normal saline, stretched by pins on cardboard, and fixed in 4% formaldehyde. After fixation and washing for 24-hour periods, the specimen was transferred at 24-hour intervals to 80, 95, and 100% alcohol, and then to equal parts of alcohol and methyl salicylate. Final clearing was done in pure methyl salicylate. The fine details in blood supply are described at length and the literature of the subject in other laboratory animals and in man is discussed. The experiments throw no light on how the deficient diets lead to ulceration.

[The photomicrographs are good and show what can be done with this sort of technique.] *Denys Jennings*

1889. **Radiological and Clinical Features of Large Gastric Ulcers.** (Röntgenologisches und Klinisches über das grosse Magengeschwür)
N. H. KRISNAPOLLER. *Gastroenterologia* [*Gastroenterologia, Basel*] **71**, 142–170, 1946. 5 figs., 52 refs.

The author discusses the large gastric ulcer, especially the diagnosis and pathological findings. Referring to large and small ulcers he points out that one may merely be a stage of the other, either in the acute or in the healing phase. In 384 cases of gastric ulcer there were 158 large ulcers, 25 of these being of the giant type, and 226 small ones. A large ulcer is defined as one measuring more than 1·5 cm. across, and a giant ulcer as one measuring more than 3 cm. across. Of 150 cases of large ulcer studied, 109 were in men and 41 in women. The incidence of gastric ulcer is highest between the ages of 40 and 50 years, but the proportion of large ulcers increases throughout life, so that while large ulcers are seen in only 20% of cases in the 20 to 30 age group they are seen in 70% of cases in the 70 to 80 age group. Large ulcers occur most often in the upper and middle parts of the stomach and never in the antrum. The size of the ulcer is no indication of the length of time it has been present, and large ulcers can change in size very rapidly. The shortest duration of symptoms in the case of small ulcers was 2 to 4 weeks, and in large ones 4 to 8 weeks. Healing is more rapid in a small ulcer, but the longer ulcers have been present the more the healing times of large and small ulcers approximate. Large ulcers more frequently leave a residual niche as seen radiologically and show a greater tendency to local recurrence. Of giant ulcers 39% are penetrating. Multiple ulcers occur infrequently and two large ulcers are never found together.

The danger of haemorrhage is greater with large ulcers, but the degree of haemorrhage does not appear to depend upon the size of the ulcer. Large ulcers often show low acid curves or even achylia. The blood sedimentation

rate is raised in about 50% of cases. The differential diagnosis of large ulcers from carcinoma can often be determined by clinical findings in conjunction with *x*-ray appearances, but in doubtful cases progressive healing of the ulcer is said to exclude malignancy. Large ulcers give no more pain than small ones if they are not deep or penetrating, but early onset of pain is more marked in the larger ulcer. With penetrating ulcer the pain is severe and radiating. The authors found, when assessing progress in cases of large ulcer, that clinical and *x*-ray findings often did not agree. *L. W. Lauste*

1890. **Gastroscopic Findings in Chronic Duodenal Ulcer**
E. J. LEFEBER. *Texas Reports on Biology and Medicine* [*Tex. Rep. Biol. Med.*] **4**, 324–337, Fall, 1946. 25 refs.

Gastroscopy was performed on 46 patients with chronic duodenal ulcer. Of these, 37 were males and 9 were females; 26 were white and 20 were negro. The ulcer was judged, on combined clinical and radiological evidence, to be active in 37 and inactive in 9. The stomach was considered normal in 20 patients, while in 26 " chronic gastritis " was diagnosed; this was classified as hypertrophic in 19, atrophic in 3, superficial in 2, and mixed in 2. No correlation was found between the symptomatology and the gastroscopic findings. The response to therapy of the 20 patients with normal stomachs was satisfactory in 12, and unsatisfactory in 8. Of the 26 patients with chronic gastritis, the response was satisfactory in 13 and unsatisfactory in 13. Although there is no significant difference between these figures, the author states that " the impression is gained from a survey of the case histories of the 46 patients with duodenal ulcer in this series, that certain patients with a gastritis are often more difficult to manage therapeutically ". In 7 patients gastroscopy was repeated after an interval of 2 to 48 months: all showed evidence of gastritis on both occasions, in spite of therapeutic measures directed towards control of the ulcer symptoms during the intervening period. The author concludes that in most patients with duodenal ulcer the demonstration of a chronic gastritis has little clinical significance.

[No indication is given of the criteria adopted in the diagnosis of " gastritis ", and no information as to the technique or type of gastroscope used: some of the examinations were made by another physician.]
A. R. Kelsall

1891. **Incidence of Ulcer in Haematemesis**
E. H. CLUER. *British Medical Journal* [*Brit. med. J.*] **2**, 651, Nov. 2, 1946. 6 refs.

Haematemesis is presumed to be almost always diagnostic of peptic ulcer or, failing this diagnosis, of oesophageal varix. Cluer, however, records that of a series of 18 patients admitted to his ward primarily for acute haematemesis only 7 gave radiographic confirmation of peptic ulceration. The usual treatment for post-haemorrhagic shock was instituted, and subsequently the Witts modification of the Meulengracht dietary regimen was begun. Drug treatment consisted of iron as ferri et ammon. cit. gr. 30 (2 g.) 3 times a day, phenobarbitone, magnesium trisilicate, and belladonna with adequate vitamins. The iron was continued long after the patients' discharge with noticeable amelioration of the blood pictures. The average in-patient period was 5 weeks, and 3 months later the radiological reports were as follows: chronic duodenal ulcer, 5; chronic gastric ulcer, 1; anastomotic ulcer, 1. Two patients had symptoms suggestive of peptic ulceration; its presence, however, was not confirmed by skiagram, and the ulcer had probably been healed by the treatment described. Two further cases were due to ruptured oesophageal varices complicating hepatic cirrhosis, while one patient with severe hypertensive epistaxis had probably vomited swallowed blood.

It is interesting that 6 patients had no dyspeptic history anterior to their episode of haematemesis, that their skiagrams were perfectly normal after treatment and that, except in one case, their test meals were within normal limits for acid. The cases must therefore be considered to have had " acute gastric erosions ". There is evidence that patients admitted with haematemesis and melaena may be suffering from active gastritis or superficial erosion. The haemorrhage in these cases may be brisk but not severe. It must be noted *per contra* that the complications of haemorrhage, perforation, or even stenosis may supervene in patients with minimal dyspeptic symptoms and may occur especially in the most acute type of ulcer. This type may heal so well as to reveal no deformity on subsequent skiagrams. Cluer points out that the treatment of haematemesis is the same whether due to an acute erosive lesion or to chronic ulcer. He raises the question whether a 33% incidence of acute gastric erosion in an admittedly small series of cases of haematemesis is an average finding or is perhaps rather high. *Arthur A. Bradley*

1892. **Paradoxical Response of Gastric Secretion to Atropine Stimulus.** (Interpretazione e significato delle reazioni paradosse della secrezione gastrica allo stimolo atropinico)
V. SCAFFIDI. *Policlinico* [*Policlinico*] **53**, sez. prat. 786–796, Sept. 12–23, 1946. 10 refs.

The effect of atropine on the fasting gastric secretion was studied by means of the stomach tube in 4 patients with symptoms of gastro-duodenal ulcer, 2 patients with hyperchlorhydria, and 1 apparently normal subject. In 1 patient with gastro-duodenal ulcer, the 2 with hyperchlorhydria, and the normal subject the administration of 1 mg. of atropine caused a paradoxical prompt stimulation of hydrochloric acid secretion, without diminution of the total volume of juice obtainable from the stomach. In 2 other ulcer cases the stimulating effect of the atropine on the secretion of acid was tardy, and accompanied by marked diminution in the volume of juice secreted. In the remaining patient with gastro-duodenal ulcer the slow increase in the acid concentration was accompanied by only a slight decrease in the volume of fluid. In none of the cases was a correlation observed between the concentration of acid and the volume of fluid secreted, but in all cases this paradoxical stimulation by atropine of the secretory vagus endings in the stomach was

accompanied by an equally paradoxical depression of heart rate and blood pressure. In almost all the cases a dose of 2 mg. of atropine produced the normal effects of inhibition of vagus endings. *T. R. Parsons*

1893. **Pyrosis. An Analysis of Its Clinical Significance and Pathogenesis**
G. W. H. SCHEPERS. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **39**, 333–338, Oct., 1946.

The author was asked by one of the largest benefit societies on the Witwatersrand, S. Africa, to examine and treat an unspecified large number of patients with chronic illness. Many were " museums of pathology ". No details of age and sex distribution are given, but there were more women than men. A common complaint was pyrosis, which is defined as an " oppressive, burning sensation below the xiphisternum, associated with acid eructations, pain at the inferior angle of the left scapula, and flatulence ". The author gives discursive information about the " first hundred cases [of pyrosis] selected at random ". The incidence of pyrosis in males was " probably relatively higher " than in females. It was commoner and more severe in the third and fourth decades. The habitus was mostly sthenic or pyknic, and 75 patients admitted recent or excessive gain in weight. Radiology showed 7 patients with duodenal ulcer, 33 with irritable duodenal caps or duodenitis, and none with gastric ulcer, while 96 normal and 4 abnormal cholecystograms were found. Irritative lesions were present in the descending colon in at least 25 patients. [Functional hiatal hernia were apparently not looked for.] There was hypochlorhydria in 84 patients but hyperchlorhydria in 6 only. Endocrine abnormalities occurred in 64 cases, especially hypothyroidism. Myxomatous deposits were demonstrable in 55. The systolic blood pressure was under 100 mm. in 54 cases and slightly raised in 36. Urinary tract infection was present in 86 patients and in 33 this was apparently confined to the upper part of the tract. Lack of libido was a common complaint, and there were many nervous symptoms, especially paraesthesiae. The author found that treatment of the renal condition and endocrine therapy were fairly successful. He suggests that pyrosis is a form of visceral paraesthesia, and that the irritability of the gut is secondary to excretion of irritants following renal damage.

[It is impossible to assess the value of this investigation as the statistical details and the findings in the control series are omitted. Observation of out-patients in Britain gives a different impression, but cases of the type mentioned by the author do occur and deserve fuller mention in textbooks.] *Denys Jennings*

1894. **Folic Acid in Tropical Sprue. Report of a Case**
P. MANSON-BAHR and O. CLARKE. *Lancet* [*Lancet*] **2**, 903–904, Dec. 21, 1946. 3 figs., 2 refs.

The case of severe and long standing sprue described has been cured by folic acid. The authors comment on the inadequacy of treatment of this disease before the use of folic acid despite intensive research in India and elsewhere during the war. The patient in question first left England for India in March, 1943. He was then aged 27 and weighed 148 lb. (66·6 kg.). In February, 1944, the stools were noted to be bulky, greasy, biscuit-coloured, and of unpleasant smell. In August, 1944, when his weight was 91 lb. (40·5 kg.), he was able to begin treatment, consisting of controlled milk and orange diets, liver extract by mouth and by injection, and nicotinic acid by mouth. Neither this treatment nor return to England restored his health. In September, 1946, he was admitted to hospital. He was thin, pale, dehydrated, and listless, with poor appetite. The skin was dry, desquamating, and inelastic; the abdomen was distended, and the tongue was smooth and sore, with marginal glossitis; typical sprue stools, passed 3 or 4 times a day, totalled 24 ounces (720 g.) daily. The red cell count was 2,430,000 per c.mm. and the haemoglobin was 50%. For the first week in hospital treatment consisted of controlled diets, predigested milk feeds, 4 ml. liver extract daily, 100 mg. nicotinic acid and 3 mg., riboflavin daily. There was no improvement. Treatment was then started with folic acid, 10 mg. daily for 5 days by mouth. On the fourth day of treatment the patient said that he felt fitter than for many months and his appetite became normal. Three days later the soreness of the tongue had ceased, the abdomen was no longer distended, and the skin had regained its normal elasticity. The stools became normal and the total weight of faeces fell to about 10 oz. (300 g.) daily. A fractional test meal the day after completion of folic acid therapy showed no free hydrochloric acid in the fasting juice, a slightly increased excretion after the meal, and rapid emptying of the stomach. A fortnight later the results were within normal limits. The weight had increased to 126 lb. (56·7 kg.) a month later. During this period the red cell count rose to 3,600,000 per c.mm. and the haemoglobin to 78%. The total dose of folic acid was only 50 mg. which contrasts with the much higher dosage used by clinicians in the U.S.A.

[Although the improvement after folic acid is remarkable, particularly in view of the fact that the patient's condition had been stationary for 2 years, it must be stressed that no period without treatment preceded its administration and that the liver injections and nicotinic acid were given again after cessation of folic acid therapy.] *Geoffrey McComas*

1895. **A Note on Bacteriological and Parasitic Studies of the Intestinal Contents of Patients with Sprue**
F. MILANES, A. CURBELO, A. RODRIGUEZ, P. KOURI, and T. D. SPIES. *Gastroenterology* [*Gastroenterology*] **7**, 306–313, Sept., 1946. 1 fig., 10 refs.

The authors are studying the response of persons with tropical sprue to synthetic folic acid and this is an interim report. The patients, 25 in number, showed glossitis, typical stools with an increased fat content, a weight loss of at least 20 lb. (9 kg.), a hyperchromic anaemia with under 2,500,000 red cells per c.mm., hydrochloric acid in gastric juice after histamine, a flat glucose tolerance curve after administration by mouth, normal serum amylase and lipase, and a blood calcium over 8·5 mg. per 100 ml. No

patient had had specific therapy within the previous 5 weeks. The faeces, curettage specimens from the rectum and colon, and small intestine contents obtained through a Miller-Abbott tube were examined for parasites, bacteria, and yeasts. The findings, which correspond to those of other authors, are tabulated in detail for each patient. Excellent therapeutic results were obtained in every case on a diet containing no meat products, fish, fowl, or cheese, with only one egg daily and occasional milk. After preliminary studies, 10 mg. of folic acid [? misprint for 100 mg.] was given daily by mouth for 45 days. Despite a clinical and haematological improvement, the incidence of parasites, bacteria, and yeasts remained " essentially unchanged ". The authors feel that their results support the theory that sprue is " essentially a nutritional disorder ".

[In the " representative " chart showing the effect on the blood count the erythrocytes rise from 1,400,000 to 2,600,000 per c.mm. in 3 weeks on 100 mg. folic acid twice daily for 14 days with a subsequent dosage of 100 mg. daily. This hardly corresponds with the claims made in the text.] *Denys Jennings*

1896. **Acute Enterocolitis and Death Resulting from a Markedly Hypertonic Enema**

S. LINDSAY. *Gastroenterology* [*Gastroenterology*] **7**, 364–370, Sept., 1946. 4 figs., 8 refs.

A case is reported of a 6-year-old girl who died 9 hours after administration of an enema of 1,000 ml. in which half a cupful each of sodium chloride, sucrose, and sodium bicarbonate had been dissolved and suspended. Similar enemata administered to 3 guinea-pigs led to death in 2, 16, and 2 hours. Two other cases are cited from the literature and also other animal experiments. The author concludes that the loss of fluid and protein into the gut resulting from injury to its mucosa and from the high osmotic pressure of the enema fluid is the factor responsible for the shock-like condition which leads to death.

Denys Jennings

1897. **Streptomycin Treatment of Intractable Ulcerative Colitis**

W. LIEBERMAN. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **46**, 2178–2179, Oct. 1, 1946. 1 ref.

The author records the clinical details of a case of chronic ulcerative colitis in a boy of 6½ years. The previous history revealed that he had suffered from coeliac disease at the age of 3 weeks, which, despite treatment, lasted until he was 3 years old. Bacteriological examinations seemed to rule out the usual intestinal infections. Treatment with sulphonamides and special diet failed to make any impression, and the deterioration was such that recourse had to be made to blood transfusion on several occasions. The condition gradually worsened until streptomycin was administered intramuscularly—150,000 units as the first dose followed by 100,000 units at 3-hourly intervals. By the third day of treatment the number of stools per day was considerably reduced, and after a week the patient was discharged greatly improved.

T. Anderson

1898. **Psychoanalytic Study of Ulcerative Colitis in Children**

M. SPERLING. *Psychoanalytic Quarterly* [*Psychoanal. Quart.*] **25**, 302–329, July, 1946. 35 refs.

It has long been recognized that ulcerative colitis occurs in nervous people, and more recently admitted that emotional conflict and stress may be directly causative. There is, however, very little literature on the psychoanalytical findings in such cases. Two cases occurring in children are described in psychoanalytical terms. In both there was marked antagonism between child and mother and the mother and child were in a severe state of anxiety and conflict. The child was frustrated and filled with rage against the mother but feared to lose her; the mother was filled with guilt feelings because of the desire to thrust out the child. The situation presents a difficult problem for the analyst, because she must treat both mother and child; in treating the child she uses the technique of Anna Freud, whereby she becomes the child's ally against the parent, and enables the patient to recognize her own unconscious strivings as the " devil " within who must be brought to order. In both cases recovery from the bodily symptoms resulted from the analysis, though the emotional situation was not entirely cleared up. The mechanism seemed to be that the mother was ambivalent towards the child, rationalizing the desire to get rid of it by insisting that it would be better away from home or in hospital. The child, continually frustrated by the mother's inconsistency, reacted with an intense need to maintain infantile dependence on the mother combined with a regression to strong oral and anal sadistic impulses against her. This gave rise to the eating difficulties, vomiting, pain, and bloody diarrhoea. Being extremely sensitive to any form of psychic tension the child failed to attain to a genital level, and so regressed to a pregenital oral and anal level. The bloody diarrhoea was worse in hospital, especially when active medical treatment was given or when the child was frustrated (a maximum of sadistic rage). The analogy between severe ulcerative colitis and melancholia is discussed. Recovery can only take place if the sadism is satisfied, exhausted, or changed by treatment. This explains why some cases of melancholia inevitably end in suicide and some cases of ulcerative colitis are fatal; it also explains why there is sometimes spontaneous recovery in both conditions.

R. G. Gordon

1899. **The Treatment of Coeliac Disease with Vitamin B Complex and Liver Extract**

E. C. ALLIBONE. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **39**, 700–702, Sept., 1946. 2 figs., 4 refs.

Twenty-three cases of coeliac disease were treated after initial investigations with daily intramuscular injections of vitamin B (4 ml.) alternating with liver extract (2 ml.). The preparations used were similar to those employed in America by May and his co-workers (*J. Pediat.*, 1941, **21**, 289). The course of treatment was carried out for 3 weeks with the first 15 cases, and for 6 weeks in the last 8 cases. No significant changes were found in the oral glucose tolerance curves or in the absorption of fat as

judged by faecal fat analyses. No other marked changes were recorded, and it is concluded that this type of therapy is not specific for coeliac disease. *A. C. Frazer*

1900. **Possible Case of Crohn's Disease in a Ruanda Native**
A. K. KIBAYA. *East African Medical Journal* [*E. Afr. med. J.*] **23**, 317–320, Oct., 1946. 2 refs.

Crohn's disease has rarely been recorded in Africans. A case is reported in an adult male Munyarwanda from Uganda. The diagnosis was confirmed at necropsy.
G. M. Findlay

1901. **Some Clinical and Pathogenic Features of Haemochromatosis.** (Étude sur quelques éléments cliniques et pathogéniques de certaines cirrhoses bronzées)
M. CREYX and J. LÉVY. *Journal de Médecine de Bordeaux et du Sud-Ouest* [*J. Méd. Bordeaux*] **123**, 321–335, Sept., 1946.

The authors recapitulate critically the classical description of haemochromatosis; they consider a degenerative hepatitis to be the primary lesion, which sooner or later is accompanied by diabetes and a localized or generalized pigmentation caused by deposition of haemosiderin. Three groups are distinguished in those cases in which diabetes is clinically absent. The first group has normal blood sugar and normal sugar-tolerance curves (pigmentary cirrhosis without diabetes), the second has a slightly raised fasting blood sugar, and the third, with normal fasting blood sugar, has abnormalities in the blood-sugar-tolerance curves, the hypoglycaemia after insulin, and the hyperglycaemia reaction after adrenaline; for the last group the name " paradiabetic pigmentary cirrhosis " is suggested. Loeper's finding of an increase in the neutral sulphur content of the blood is briefly discussed. The authors' own observations are based on 11 cases. All had hypertrophic cirrhosis, predominantly affecting one lobe; signs of abnormal collateral circulation were absent. Necropsy in 4 cases showed absence of peritoneal effusion. The spleen was moderately and never grossly enlarged, and the rarity of haemorrhagic phenomena is stressed. Liver function tests were of little use. The diabetic element showed peculiar features in 3 cases: in the first, diabetes disappeared for 2 years, reappeared, and remained until the patient's death; the second case was that of an alcoholic who died in hypoglycaemic coma which proved refractory to treatment; the third patient died in a rapidly developing coma in similar circumstances to Case 2. In a certain proportion of cases congestive heart failure of unknown origin is the presenting feature; it is characterized by persistent tachycardia, gallop rhythm, low blood pressure, and disturbances of auriculo-ventricular conduction. Its occurrence seems more than a coincidence and the deposition of pigment in the fibres of the myocardium may form its anatomical basis. The relation of endocrine glands to haemochromatosis has been discussed by various authors; the case is briefly reviewed of a patient with infantilism and haemochromatosis in which deposits of haemosiderin in several endocrine organs were found. It is assumed that endocrine disturbances preceded the appearance of haemochromatosis in this case as well as in a personal case, that of a man aged 42, alcoholic, with a complex congenital malformation of the genital organs, grossly enlarged liver, bronzed pigmentation of the face, and slate-coloured discoloration of the skin elsewhere. It is pointed out that, while several aspects of some published cases of haemochromatosis point to an endocrine aetiology, this is not more than a hypothesis.

[The authors' case does not appear to be a convincing example of haemochromatosis of endocrine origin, as such an origin of the congenital malformation is doubtful, glycosuria was absent, and the blood sugar normal.]
A. Schott

1902. **Diagnosis of Liver Abscess by means of Thorotrast Hepatosplenography**
R. J. REEVES and K. A. YOUNGSTROM. *Texas State Journal of Medicine* [*Tex. St. J. Med.*] **42**, 310–314, Sept., 1946. 3 figs., 9 refs.

The highest incidence of liver abscess is found in amoebiasis. Usually the liver is enlarged, although if the abscess is small and deeply situated, the liver may appear externally normal. If the abscess lies near the capsule, there is usually localized peritonitis with fibrinous exudate. If the abscess is located in the dome of the liver there are adhesions to the diaphragm and a bulging upwards of the latter. Amoebic abscess should always be considered in a patient presenting a low-grade daily remittent or intermittent fever with pain and tenderness over the liver area. Rigors and fever are more common with pyogenic abscess. Repeated stool examinations should be made for *Entamoeba histolytica*. Differential diagnosis includes cysts and metastatic and primary tumours of the liver cells, bile ducts, or other tissue elements of the liver.

When the abscess is situated centrally, the liver in the early stage may show no marked enlargement, and in such cases the use of thorium dioxide (" thorotrast ") is a valuable aid to location by *x*-ray examination. Although the drug is slowly excreted and may persist in the body for many years, no evidence has been obtained of any damage to the liver through low-grade radioactivity. Thorotrast hepatosplenography should, however, be reserved for patients where a real and useful diagnostic response can be expected. The average dose is 75 ml. colloidal thorium dioxide mixed with several hundred ml. of isotonic solution of sodium chloride. This is injected slowly intravenously over a period of 30 minutes. The reaction is very mild. In making the injection it is important to avoid infiltration into the subcutaneous tissues as otherwise the thorium is not absorbed and produces a hard painful mass. In the liver, the presence of thorium may be noted some hours after injection, *x*-ray examination showing sufficient contrast to outline a cavity or mass. The concentration of the drug in the reticulo-endothelial cells continues over several weeks and the liver density increases. Since a liver abscess or tumour is devoid of active reticulo-endothelial cells, it will contain none of the thorium dioxide and will be of lesser density than the surrounding normal liver tissue. In this manner the abscess may be easily demonstrated and accurately located.

In the present series, amoebic abscess was found to be the more common cause of liver abscess. Pyogenic abscess was primarily the complication of an intra-abdominal suppurative process with the causative organism in the portal area, the most frequent lesion being appendicitis. There is apparently no more reliable laboratory method, short of operation, for differentiating between carcinoma and cirrhosis in an enlarged liver than the use of thorotrast. *F. Murgatroyd*

1903. **Hemochromatosis. Review of Literature and Presentation of a Case Without Pigmentation or Diabetes**
C. CHESNER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 1029–1036, Sept., 1946. 3 figs., 19 refs.

The author describes an unusual case of haemochromatosis without pigmentation of the skin and without diabetes in a white boy of 14 years. He bases the diagnosis on the findings post mortem of a pigment cirrhosis of the liver, fibrosis and pigmentation of the pancreas, and siderosis of other organs. The liver at necropsy contained 47 g. of iron. Splenomegaly was also a feature, and the spleen was removed when the initial diagnosis of Banti's disease had been made. This was followed by an unusually high level of blood platelets and of megakaryocytes in the bone marrow. Another unusual feature was the presence of a severe hypochromic microcytic anaemia of the iron-deficiency type which preceded the onset of other symptoms by 6 years. In a brief revue of the literature the author points out that cases of haemochromatosis have been reported in patients in whom the diagnosis of aplastic anaemia has also been made. *R. Winston Evans*

1904. **Biochemical Investigations in Liver Disease: Some Correlations with Hepatic Histology**
S. P. V. SHERLOCK. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 523–544, July, 1946. 12 figs., 36 refs.

In the past biochemical methods for the assessment of liver diseases have been based either on animal experiments or on cases of liver diseases verified by operation or at necropsy. In this paper a more exact evaluation of various liver tests is obtained by aspiration biopsy. Biochemical tests used were estimations of the serum bilirubin, alkaline phosphatase, cholesterol, and proteins. In addition the patients were submitted to the intravenous galactose tolerance and the hippuric acid synthesis tests. Liver disease in 187 patients was investigated; of these patients 84 were considered to have acute hepatitis. This group comprised 21 cases of infective hepatitis, 9 of serum jaundice, and 54 of jaundice following intravenous arsenic therapy for syphilis. Histologically it was not possible to differentiate the aetiogical factor concerned, since in each the lesion was essentially an acute inflammation with varying degrees of cell necrosis. The degree of cell necrosis proved to be helpful, because it was found possible to compare the amount of cellular damage with the chemical findings. Four arbitrary grades were taken which merged one into another; grade A (26 cases) showed 75 to 100% of surviving cells; grade B (39 cases) 50 to 75%; grade C (14 cases) 25 to 50%; and grade D (5 cases) less than 25%.

In acute hepatitis it was found that the serum bilirubin level ran parallel with the severity of the liver lesion. A serum bilirubin of more than 10 mg. per 100 ml. was usually associated with severer grades of liver damage. The serum phosphatase rarely exceeded 30 units per 100 ml., and, unlike the serum bilirubin, could not be taken as a guide to the degree of cell necrosis. The serum cholesterol, serum protein, albumin, and globulin levels were always within normal limits and gave no diagnostic aid. The intravenous galactose test, which consisted of the injection of 0·5 g. of galactose per kilo of body weight, was assessed by the time taken for this substance to disappear from the blood stream. This test, in contradistinction to the hippuric acid synthesis test, gave a reliable index of the degree of liver damage. In the recovery stage of acute hepatitis the rapidity of fall of serial bilirubin readings was inversely proportional to the severity of the lesion found at liver biopsy. The serum phosphatase, on the other hand, did not show the steady fall characteristic of the serum bilirubin, though in general the patient in grade D took the longest time for the serum phosphatase to reach normal. Again the estimation of the proteins did not give any diagnostic aid. Both the hippuric acid synthesis test and the galactose tolerance test had returned to normal before the hyperbilirubinaemia had ceased.

In hepatic cirrhosis the investigations in the inactive stage revealed no consistent abnormality. In the active stage a fluctuating bilirubin level was found, although this was not grossly raised in any of the 17 patients examined. The galactose and hippuric acid synthesis tests were always abnormal. The former showed impairment which was in proportion to the extent of cell necrosis. In obstructive jaundice there was an upward trend of both the serum bilirubin and serum phosphatase. The serum phosphatase in this type of disease almost invariably exceeded 30 units per 100 ml. and served as a good diagnostic point. The total proteins were frequently found to be lowered at the expense of the albumin, which, in 7 cases out of 12, was less than 3·0 g. per 100 ml. The galactose tolerance and hippuric acid synthesis tests were usually impaired. In a small group of miscellaneous diseases involving the liver the biochemical studies generally gave normal or equivocal results.

In the discussion the author points out the difficulties with which the clinician is faced by a battery of liver function tests. She draws attention to the fact that liver disease is often accompanied by renal disease and this adds to the confusion of a " shotgun " type of biochemical investigation. As the result of this work she considers that only the serum phosphatase estimation and intravenous galactose test gave a true indication of the liver damage. *E. M. Darmady*

1905. **Antral Gastritis and Spasm: Their Clinical and Surgical Significance**
J. W. R. RENNIE. *Annals of Surgery* [*Ann. Surg.*] **124**, 402–409, Aug., 1946. 7 figs., 15 refs.

Endocrine Disorders

1906. **Phenomenon of Functional Exhaustion of Certain Endocrine Organs (Thyroid Gland and Anterior Lobe of Pituitary Body).** [In English]
A. A. WOITKEWITSCH. *Comptes Rendus (Doklady) de l'Académie des Sciences de l'U.R.S.S.* [*C. R. Acad. Sci. U.R.S.S.*] **51**, 729–732, 1946. 6 refs.

During the seasonal moult and the growth of new plumage in birds the thyroid gland increases its function. This fact was used to test the state of the thyroid. The feathers of carrier-pigeons were plucked at successive intervals, and some of the birds were killed 12 days after each plucking. Half of the animals received 100 mg. "thyroidin" daily. Histologically the thyroid glands after the first and second plucking appeared to be hyperactive, as seen from the height of the epithelial cells, whereas after the third plucking the follicle cavity had disappeared; the implantation of such glands into tadpoles did not influence their metamorphosis. This is taken as a sign of exhaustion of the gland. The thyroidin-fed birds behaved normally.

In the case of the basophilic cells of the anterior pituitary exposure to electric light for from 3 to 48 days has been used as a stimulus in frogs, toads, and land tortoises. In the beginning of the exposure to light the thyrotrophic action of the pituitary was increased, but in the later stages the function of the thyroid gland went back to normal, and the basophilic cells diminished in size and granules disappeared. This is regarded as a sign of exhaustion. *H. Herxheimer*

1907. **The Influence of Unilateral Nephrectomy on the Weight of the Endocrine Organs in Mice.** [In English]
M. WRETE. *Acta Anatomica* [*Acta anat.*] **2**, 81–97, 1946. 10 refs.

Gaarenstroom (*Act. brev. neerl. Physiol.*, 1942, **12**, 107) showed that, after hypophysectomy, unilateral nephrectomy was not followed by compensatory hypertrophy of the remaining kidney, and that after thyroidectomy and unilateral nephrectomy the compensatory hypertrophy was less than usual. Following up this work the present author has investigated the changes in weight of the endocrine organs in a series of white mice on which unilateral nephrectomy had been performed.

Of 50 male white mice, aged 4 months, 24 were weighed and the right kidney of each removed and weighed. The rest of the animals served as controls. All were killed with ether 1 month later; the total body weight was determined, and the brain, hypophysis, thyroid, adrenals, gonads, and thymus were removed and weighed, the right and left adrenals together, the remainder separately. Organs from 4 nephrectomized and 4 control animals were fixed in formalin-sublimate, stained, and sectioned; all other organs were dehydrated at 110° C., and the dry weight determined. Final body weights of the nephrectomized group included the weight of the extirpated kidney. Precise comparison between experimental and control animals was not possible as controls were not weighed at the beginning of the experiment. The mean body weight of the nephrectomized animals increased by about 6·7% during the experiment, and was about 9·5% above that of the controls at the end of the experiment. The mean wet weights of the brain and the majority of the endocrine organs of the experimental animals were greater than those of the controls by amounts of the same order as this latter figure. The hypophysis and the thyroid gland, however, showed a great and significant increase—23·4% for the former and 12·7% for the latter. The mean brain weight is more constant than the mean body weight, and in the nephrectomized group was 7·1% above that of the control group. Expressed as a percentage of the mean brain weight the mean weight of the hypophysis in the nephrectomized group was 31·5% greater and that of the thyroid 19·2% greater than the corresponding weights in the control group. These figures are statistically significant. The dry weights of the organs show little variation. To exclude the possibility that the mere loss of a considerable mass of tissue might induce hypertrophy of the hypophysis and thyroid the author amputated the tail in 29 animals out of a group of 59, the remainder serving as controls. Body weights were ascertained before operation, the tails being weighed after operation and their weight added to the total body weight at death. Both groups showed percentage increases in body weight of about 8%. There was no significant rise in the mean weight of any endocrine organ.

The author concludes that the rise in the mean weight of the hypophysis and the thyroid is statistically significant, and that it suggests a direct relation between the activity of these glands and the hypertrophy of the remaining kidney. *H. Hughes*

1908. **Structural Analogues Antagonistic to Thyroxine**
D. W. WOOLLEY. *Journal of Biological Chemistry* [*J. biol. Chem.*] **164**, 11–17, July, 1946. 6 refs.

Many compounds related structurally to important metabolic vitamins and hormones are now known to inhibit the action of the physiologically active compound which they resemble and thus to produce signs of specific deficiency. The author has synthesized several compounds closely related to thyroxine, and has shown that some of them inhibit the toxic action of thyroxine on tadpoles. When tadpoles of 3 to 4 cm. in length are immersed in solutions of thyroxine of sufficient strength they undergo rapid metamorphosis and die; this metamorphosis is prevented if certain thyroxine analogues are added to the solution. Several ethers of N-acetyldiiodotyrosine were prepared and found to protect tadpoles against the lethal action of thyroxine; they also antagonized the effect of the hormone in causing an

increased rate of metamorphosis in these animals. The *p*-nitrophenylethyl ether of N-acetyldiiodotyrosine was the most efficient in protecting against the lethal action of thyroxine as well as in antagonizing the effect of the hormone in increasing the rate of metamorphosis. The *p*-nitrobenzyl ether was almost as effective, while the benzyl and trilyl ethers were less active. N-acetyldiiodotyrosine and *o*-methyl-N-acetylthyroxine were inactive. In the absence of thyroxine some of the thyroxine analogues, notably the *p*-nitrophenylethyl ether were toxic to tadpoles. The nitro ethers could be shown, in the absence of thyroxine, to have a weak thyroxine-like action on tadpoles and mice as well as an antithyroxine activity. *J. Dawson*

1909. **On the Problem of Extra-Thyroid Formation of Thyroxine in Hypothyroidic Patients.** [English Summary] H. ZONDEK. *Harefuah* [*Harefuah*] **31**, 133–134, Oct. 15, 1946. 2 figs., 18 refs.

According to reports of a number of authors, iodine is able to form compounds with body proteins with a thyroxine-like action in thyroidectomized animals. The aim of the present work was to shed light on the corresponding conditions in man so as to supplement former investigations. In the case of a 41-year-old woman suffering from severe primary myxoedema (her thyroid did not respond at all to administration of thyreotropic hormone) and requiring about 0·6 to 0·8 g. thyroidine daily, withdrawal of thyroidine was repeatedly followed by the recurrence of severe myxoedematous symptoms. It was shown that iodine plus iodide in doses varying from 0·01 to 0·30 g. a day could not replace thyroid hormone in any way. In the human body with its highly differentiated thyroid tissue extra-thyroid formation of iodized proteins with thyroidin-like effect does not seem possible. Likewise no thyroidin-like effect resulted from the administration of di-iodo-tyrosine, i.e., no transformation of di-iodo-tyrosine into thyroidine could be brought about. Neither have protenogen amines such as tyramine any effect on the human thyroid as was demonstrated in former investigations.—[Author's summary.]

1910. **Studies on the Effect of Thiourea and Allied Substances on the Thyroid Gland and Other Organs in Rats and Mice**
R. P. JONES. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 483–493, July, 1946. 15 figs., 16 refs.

Toxicity tests by a single oral dose in mature rats showed LD 50 to be 25 to 30 mg. per kilo for α-naphthyl thiourea, 160 to 180 mg. per kilo for β-naphthyl thiourea, and >180 mg. per kilo for αα-dinaphthyl and ββ-dinaphthyl thiourea. Repeated oral doses in rats and subcutaneous injections in mice gave an LD 50 for thiourea of >1,000 mg. per kilo.

Twenty mg. of α-naphthyl thiourea per kilo caused oedema of the lungs, the volume of fluid ranging from 2·72 to 1 ml. 5 hours after administration and from 13 to 5·6 ml. after 24 hours, decreasing to 5·2 ml. by the second day and to 1·3 ml. by the fourth day. Evidence of oedema was also found at necropsies on animals given β-naphthyl, αα-dinaphthyl, and ββ-dinaphthyl thiourea. Changes in the endocrine glands were found only after giving thiourea and α-naphthyl thiourea. The pituitary showed no change 5 hours or 2 and 3 days after a single dose of 20 mg. of α-naphthyl thiourea per kilo, nor after 9, 12, 13, 15, and 17 doses of 10 mg. per kilo. There was no histological change in the adrenal glands. The difference between the mean adrenal weight of rats receiving 33 doses of 10 mg. per kilo (0·515 g.) and that of controls (0·68 g.), and in weight of the testes (1·156 and 1·225 g. respectively), was not significant. The weight of the thymus after this dosage was decreased (0·12 g. compared with 0·32 g.). [No organ weights are given after thiourea treatment.]

Both α-naphthyl thiourea (lowest effective dose, 20 mg. per kilo) and thiourea (1,000 mg. per kilo) produced histological changes in the thyroid gland. There was a reduction of colloid, the epithelium was high cuboidal, columnar, or high columnar, and the nucleus was chiefly basal. Hypertrophy of the thyroid gland resulted only after 20 oral doses of 1,000 mg. of thiourea per kilo given over a period of 23 days. [No thyroid weights, numbers of cell types, or measurements of cell height are given.] All types of Golgi apparatus were to be found in control rats and in those given α-naphthyl thiourea; after thiourea, cells with large vacuoles and fragmented Golgi apparatus were absent, those with a hypertrophied Golgi apparatus in the form of a loose network predominating. There were no consistent changes in the thyroid glands of mice injected subcutaneously with either 500 mg. or 1,000 mg. of thiourea per kilo (10 injections). Tadpole experiments were inconclusive. There was a loss of pigmentation in those kept in 0·001 and 0·005% solutions of α-naphthyl thiourea, while those kept in 0·033% solution of thiourea were smaller than the controls and showed frequent tail abnormalities, but in the latter the hind-limb buds were absent. Feeding tadpoles with thyroid from control rats, from those given 10 mg. of α-naphthyl thiourea per kilo daily for 10, 12, 14, 16, and 18 days, and from rats given 8 oral doses of 1,000 mg. of thiourea per kilo over a period of 20 days gave results indicating that there was sufficient activity left in the thyroid glands of the treated animals to accelerate development, but the results were not sufficiently clear to allow any definite conclusions as to the amount of thyroxine present.
S. A. Simpson

1911. **Morphological Examination of the Blood and Sternal Marrow of Nine Patients Treated with Thiouracil**
C. J. GESSLER. *Blood* [*Blood*] **1**, 407–410, Sept., 1946. 1 fig., 1 ref.

The blood and bone marrow were studied in 9 patients receiving thiouracil for hyperthyroidism. In 2 the peripheral leucocyte count fell to below 3,000 per c.mm.: 2,500 with 875 neutrophils per c.mm. in one, and 2,500 with 1,225 neutrophils per c.mm. in the second. The first patient had taken 47·4 g. of thiouracil in 76 days, and the second 31 g. in 31 days. In both patients differential counts on sternal-marrow films, taken presumably

during the leucopenic phase, showed an increased percentage of the less mature elements of the myeloid series, particularly of the myelocytes and premyelocytes; nuclear abnormalities, toxic granulation, and vacuolation were seen in occasional cells. Erythropoiesis was unaffected. The changes are interpreted as indicating impaired development of the granular series, and it is suggested that if they had been allowed to progress a toxic agranulocytosis might have developed. This type of leucopenia is related to the total dosage of toxic substance and differs from acute allergic agranulocytosis.

R. Bodley Scott

1912. **Sternal Marrow Studies in Thyrotoxicosis Treated with Thiouracil and Review of Literature Regarding Thiouracil Effects on Blood**

S. H. SIKKEMA, E. W. THEWLIS, and O. C. MEYER. *Blood* [*Blood*] **1**, 411–425. Sept., 1946. 1 fig., 59 refs.

The authors review the literature dealing with the blood changes in thyrotoxicosis and with the effects of thiouracil on the blood and bone marrow, adding observations of their own. The mean of the blood counts in thyrotoxic patients is within normal limits, but the variability is greater; many have reported lymphocytosis, but the present authors find no constant change but slight monocytosis, which disappears with iodine. The literature contains references to 1,914 cases of thyrotoxicosis treated with thiouracil; 44 (2·3%) of these developed agranulocytosis, which was fatal in 15 (34%), and a further 93 (4·9%) had significant leucopenia. Agranulocytosis might appear at any time from 2 to 36 weeks after starting treatment, but was most frequent from the fifth to the eighth week. The ages of patients affected varied from 16 to 70 years.

The authors have studied 27 patients with thyrotoxicosis, 7 receiving thiouracil, 18 iodine, and 2 both drugs. Examinations of blood and sternal bone marrow were made before and after treatment, and in 14 cases after thyroidectomy. No significant deviations from the normal were found except in 2 of the patients receiving thiouracil. One developed agranulocytosis during her third course of thiouracil; the total leucocyte count fell to 1,000 per c.mm. and neutrophils were absent. Sternal puncture at this stage showed 9·2% myeloblasts but no other cells of the granular series. With crude liver extract, pentnucleotide, blood transfusion, and yellow bone marrow extract the total leucocytes rose in 7 days to 16,000 per c.mm. and sternal-marrow films showed large numbers of immature granular cells, myelocytes and young-form neutrophils predominating. The patient died in thyroid crisis. In the second case the leucocytes fell, after 3 weeks of thiouracil treatment, to 1,700 per c.mm. with 18% neutrophils; sternal-marrow films showed a great reduction in the less mature granular elements. After 2 days' treatment with penicillin, pentnucleotide, and blood transfusion the leucocytes rose to 4,700 per c.mm. and the sternal marrow had returned to normal.

The authors conclude that their cases favour Plum's view that in agranulocytosis the primitive granular cells disappear from the marrow first, and are the first to reappear in the recovery phase. Their observations are opposed to the concept of "maturation arrest". Agranulocytosis develops with alarming rapidity during thiouracil treatment, but 2 or 3 days of slight leucopenia often precedes the profound fall. They consider hypersensitivity unlikely to be operative in this type of agranulocytosis, but time and dose may be of importance. They recommend blood counts 3 times weekly for all patients taking thiouracil, and daily if there is any suggestion of granulopenia. *R. Bodley Scott*

1913. **Influence of Methylthiouracil upon the Content of Hormone in the Thyroid Gland.** [In English]

J. M. KABAK and A. FRIDMAN. *Comptes Rendus (Doklady) de l'Académie des Sciences de l'U.R.S.S.* [*C.R. Acad. Sci. U.R.S.S.*] **51**, 733–736, 1946. 1 fig., 14 refs.

Rats, 60 g. in weight, received 3 mg. of methyl thiouracil a day, and their thyroids were implanted after varying intervals into tadpoles. It was found that these thyroid glands lost their ability to provoke metamorphosis in the tadpoles. It is concluded that the metamorphogenetic substance within the thyroid hormone is decreased under the influence of the drug. *H. Herxheimer*

1914. **Propyl Thiouracil in the Treatment of Hyperthyroidism**

E. P. MCCULLAGH, E. J. RYAN, and R. SCHNEIDER. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **13**, 232–236, Oct., 1946. 3 figs., 1 ref.

Thiouracil has placed the medical treatment of thyrotoxicosis, both primary (Graves's disease) and secondary (adenomatous goitre), on a secure basis. It has been used with signal success in all forms of thyrotoxicosis, either as the sole method of treatment or in combination with other drugs, and in the pre-operative preparation of those for whom surgery is thought to be indicated. Its slow action makes it unsuitable for the management of crises in which iodine, sedation, refrigeration, oxygen, blood transfusion, and other adjuvants are indicated. Objections to the general use of thiouracil are: (1) its toxic effects, especially the risk of agranulocytosis, which may occur in as many as 3% and is fatal in half of these — a mortality comparable with that of surgery in expert hands; and (2) the lack of knowledge of the frequency of recurrence of symptoms following cessation of treatment. These have weighted opinion in the authors' clinic in favour of surgery. Astwood, who introduced propyl thiouracil in May, 1946, reported its use in 100 cases of thyrotoxicosis without any noteworthy toxic reactions being observed. Among over 500 patients who are now known to have been treated with this drug there has been only one instance of agranulocytosis, and this occurred in a patient known to have had agranulocytosis on previous occasions. Recovery followed the generous use of penicillin.

In this paper the authors record the results of an 8-months' trial of propyl thiouracil in a series of 110 cases. Of these, 4 had had toxic reactions to thiouracil demanding withdrawal of the drug; 3 of these took propyl thiouracil without untoward effect; 1 had a mild sore

throat and a fall in neutrophil leucocytes of 22%. It is advised that treatment be continued for 6 to 9 months after the basal metabolic rate has become normal. Almost all patients can be up and about during treatment, and most can continue at their usual tasks, but in some sedation and extra rest are helpful, and where cardiac decompensation is evident the appropriate measures—rest, digitalis, mercurial diuretics—may be necessary. In some patients a thrill and bruit appeared over the thyroid during treatment, but disappeared promptly with 10 mg. of iodine daily, which does not apparently interfere with the action of propyl thiouracil.

There is with propyl thiouracil, as with thiouracil, an extremely wide variation in the rate of response. In some patients the basal metabolic rate fell more than 1% daily, while in others no response was evident for months. The most favourable cases are those of short duration, those with a small thyroid gland, and those in which there has been no prior iodine medication; but the authors are investigating the possibility of combining speed of response (iodine) with safety of prolonged control (propyl thiouracil). The initial dose tried was 75 mg. daily, but where there was no rapid response the dose was increased to 200 to 300 mg. per day. The authors now advise starting treatment with 200 mg. daily in divided doses. Finally they claim that propyl thiouracil may well become the treatment of choice in thyrotoxicosis, surgery being reserved for pressure symptoms, possible malignancy, or disfigurement.

[The propyl thiouracil used is evidently the 6-*n*-propyl thiouracil described by E. B. Astwood and W. P. Van der Laan (*J. clin. Endocrinol.*, 1945, **5**, 424).]

Henry Cohen

1915. **The Effect of Thiouracil Hypothyroidism on Reproduction in the Rat**

G. E. S. Jones, E. Delfs, and E. C. Foote. *Endocrinology* [*Endocrinology*] **38**, 337–344, June, 1946. 2 figs., 2 refs.

Fourteen male and 15 female adult rats had their drinking water replaced by 0·1% thiouracil solution: the average daily intake of the drug was 24 mg. in the males and 20 mg. in the females. Treatment was continued for from 49 to 340 days, and thyroid hyperplasia was produced in all cases. The increase in thyroid weight was greater in the males; the highest weight was 170 mg., against 42 mg. in the females.

Six male rats successfully sired litters after 49 days' treatment, but of 16 attempted matings after 166 to 259 days of treatment only 8 were successful. The failures could, however, be attributed to illness, or were in rats which mated successfully in later attempts. There appeared to be some prolongation of the gestation period, which averaged 31 days, excluding two of 57 and 94 days. [No control data of mating or gestation records for the colony are given.]

Nine females treated for 84 days all mated successfully, but 4 resorbed their litters; resorption of litters occurred in all of 18 matings made after 126 to 202 days of treatment.

While the upsets in male fertility are attributed to the general toxic effects of the drug, the resorption of the litters in the females is attributed to the induced hypothyroidism. The mechanism of this effect is discussed, and it is suggested that faulty utilization of oestrogen and/or progesterone in thyroid deficiency leads to a relative deficiency of one or both, so that pregnancy cannot be maintained. *Peter C. Williams*

1916. **The Connexion between Thyroid Gland Function and Tendency to Thrombosis.** (Beitrag zum Zusammenhang zwischen Schilddrüsenfunktion und Thromboseneigung)

L. Á. Pálos and L. Bozóky. *Wiener Zeitschrift für Innere Medizin* [*Wien. Z. inn. Med.*] **27**, 457–460, Oct., 1946. 1 fig., 9 refs.

It is a well-known fact that patients suffering from Graves's disease rarely suffer from thrombosis after operation; on the contrary, they often show a tendency to post-operative haemorrhage. Furthermore, thromboses are more common in the obese, somewhat hypothyroid type of patient. The case is described of a man who had suffered from typhoid fever 23 years ago, complicated by thrombosis in both legs. This patient, now aged 42, had developed 15 venous thromboses during the past 3 years. Thorough clinical and biochemical examinations were carried out; the only two abnormalities found were a clotting time of 10 seconds (normal, 5 minutes) and a prothrombin time of 45 seconds (normal, 50 seconds). He was treated with anticoagulants for a fortnight without any lasting effect. It was then decided to try thyroid treatment. After 2 months the clotting time returned to normal and the prothrombin time was 64 seconds. The thyroid was not administered continuously but intermittently in decreasing doses. The patient has had several courses of treatment, and has remained well without any thrombosis during the past 2½ years. Thyroid was also administered, without any beneficial result, to a number of patients suffering from thrombophlebitis. The authors advance the suggestion that it is only useful in cases in which the wall of the blood vessel is normal and the derangement is primarily in the blood chemistry.

[In the case described the preparation and the exact dosage of thyroid used are not stated, but from an accompanying chart they appear to be tab. thyroid. sicc. gr. 1½ (0·1 g.) daily.] *H. Jaslowitz*

1917. **Exophthalmic Goiter in Males.** [In English]

K. Larsen. *Acta Medica Scandinavica* [*Acta med. scand.*] **125**, 78–81, Aug. 1, 1946. 2 figs., 8 refs.

The number of patients with exophthalmic goitre in the Medical Department B of the Rigshospital, Copenhagen, has been unusually large in recent years; the increasing incidence has been relatively greater in men than in women. In the 4-year period 1933–6, 175 patients were discharged, of whom 22 (12·6%) were men. In the 4-year period 1941–4, 280 patients were discharged, of whom 59 (21·1%) were men. A survey of the annual reports from 7 medical clinics in Denmark likewise showed a greater increase among men than among

women. The previously accepted ratio of 1 man to every 10 patients with exophthalmic goitre had now become 1 man to every 6 or 7 patients. The relatively greater increase among males was partly accounted for by an increase in the number of masked cases, which have recently aroused more interest and may therefore be recognized more often. The age on admission of the author's 81 male patients was compared with that of female patients picked out arbitrarily. There was no difference in the average age of the two groups, but the age distribution showed a characteristic difference between the sexes. For the males the maximum incidence was in the 40–49 years age group, whereas the female patients were distributed evenly over the age groups of 20 to 59 years.

The subject of masked exophthalmic goitre is discussed in some detail; broadly the term is used to embrace those cases in which the more striking symptoms of exophthalmic goitre are unobtrusive or overshadowed by the symptoms of coincident disease. The incidence of masked exophthalmic goitre was greater in men (32·1%) than in women (11·8%). *K. Black*

1918. **Effect of Vitamin P on the Thyroid in Guinea-Pigs**
H. Cotereau, M. Gable, and J. L. Parrot. *Nature* [*Nature, Lond.*] **158**, 343, Sept. 7, 1946. 3 refs.

After the addition of 2 mg. of ascorbic acid a day to the scorbutigenic diet of male guinea-pigs (body weight 250 g.) an activation of the thyroid to the T-stage of Heyl and Laqueur (*Arch. int. Pharmacodyn.*, 1934, **49**, 838) was observed. Controls showed the Q to R stage. On a normal diet with the addition of 1 mg. of *d*-catechin epimers (used as a type of vitamin P) daily the thyroid was found to be in the resting condition (P-stage) on the fifteenth day. This is probably due to a sparing effect of vitamin P on ascorbic acid.

T. R. Parsons

1919. **Graves's Disease Accompanied by Myopathy Cured by Aminothiazole.** (Myopathie révélatrice d'une maladie de Basedow et curable par l'aminothiazol)
R. Froment, L. Gallavardin, and A. Devic. *Journal de Médecine de Lyon* [*J. Méd. Lyon*] **27**, 741–742, Oct. 20, 1946.

The case is reported of a woman, aged 47, with a history of weakness in the legs and wasting (20 kg.) of a few months' duration. She had some tremor of the limbs, a pulse rate of 120, and a moderate diffuse vascular goitre. Blood pressure was 155/90, and basal metabolic rate +39%. There was no evidence of disease of the nervous system, but weakness of the legs was so extreme that the patient could hardly move them in bed. A diagnosis of Graves's disease and myopathy was made on these findings, and was supported by biopsy of the quadriceps muscle, which showed no muscle changes with ordinary staining methods. There was multiplication of the nuclei of the sarcolemma, and certain muscle-fibre changes were found when preparations to show mitochondria were used. Estimations of the chronaxia values of the leg muscles were found to be high. A course of treatment with aminothiazole, 0·1 g. 4 or 5 times a day, was then given, and after 3 weeks the basal metabolic rate was +20%, and the pulse rate 85 per minute. There was considerable improvement in the muscular weakness and the chronaxia figures were reduced. The patient's weight, however, had not increased. A subtotal thyroidectomy was performed after 5 weeks; more aminothiazole was given, and was held to be responsible for the jaundice that appeared after 7 g. had been administered in 15 days. The relief of symptoms has persisted since operation [but it is clear that this period of observation cannot have been more than a few weeks].

S. H. Cookson

1920. **Suggested Method for Testing the Function of the Suprarenal Cortex.** (Ricerche sulla funzionalità corticosurrenale—Proposta di un metodo di esplorazione funzionale)
R. Pachioli. *Clinica Pediatrica* [*Clin. pediat., Bologna*] **27**, 202–220, July, 1946. 36 refs.

The author suggests a method of investigating the function of the suprarenal cortex in cases of slight cortical insufficiency, by determining the "substitutive" effect of parenterally administered desoxycorticosterone in causing retention of chloride. The volume of urine and the chloride excreted in the 4 hours following the administration of water (2% of body weight) is determined, and 2 days later the observations are repeated 2 hours after the intramuscular injection of 0·25 mg. of desoxycorticosterone acetate per kilo of body weight. In 8 healthy children (aged 7 to 11 years) the injection of desoxycorticosterone produced a mean fall in chloride excretion of 0·41 g. (14·6%), measured as sodium chloride; the results ranged from an increased excretion of 0·04 g. of chloride to a diminished excretion of 0·7 g. in the 4-hour period. This test was carried out on 3 groups of children with clinical signs suggestive of cortical insufficiency. The first group of 10 children suffered from severe toxic diphtheria. The observations were made 5 to 24 days after the onset of the illness, cases in which myocardial involvement was evident being excluded. The second group consisted of 7 children with severe whooping-cough uncomplicated by bronchopneumonia. The last group contained 9 children convalescent from typhoid without renal or myocardial involvement. In the diphtheria group the administration of desoxycorticosterone caused a mean fall in chloride excretion of 0·77 g. in the 4-hour test (range, 0·21 to 1·61 g.); in the whooping-cough group the mean fall was 0·6 g. (range, 0·12 to 0·9 g.); and in the typhoid group the mean fall was 0·64 g. (ranging from an increased excretion of 0·1 g. to a diminished excretion of 1·48 g.). The administration of desoxycorticosterone was considered to have exercised a "substitutive" effect in 4 cases of diphtheria and 1 of convalescent typhoid in which it produced a diminution in chloride excretion of 0·93 g. or more. Thus the author considers the method suitable for investigating mild degrees of insufficiency of the suprarenal cortex. *F. A. Langley*

1921. **Adrenal Apoplexy Associated with Hypertension**
R. L. MacMillan. *Lancet* [*Lancet*] **1**, 177–178, Feb. 1, 1947. 2 figs., 20 refs.

A man of 60 with hypertension was admitted with abdominal pain slightly suggestive of coronary thrombosis. The temperature rose and the blood pressure fell gradually, and the patient died 72 hours after the onset of the illness. Necropsy showed massive haemorrhage into both adrenal glands. A classification of adrenal haemorrhage is suggested. *H. Herxheimer*

1922. **Hormonal Modification of Social Behaviour. II. The Effects of Sex-hormone Administration on the Social Dominance Status of the Female-Castrate Chimpanzee**
H. C. Birch and G. Clark. *Psychosomatic Medicine* [*Psychosom. Med.*] **8**, 320–331, Sept.–Oct., 1946. 35 refs.

The work reported here was done to see whether the increase in dominance during the oestrogen phase of the cycle in the female chimpanzee as reported by Crawford and Yerkes occurred in castrated females receiving oestrogen or whether they would behave as castrated males, in which dominance, as determined by the food-competition test, decreased during oestrogen and increased during androgen administration. Three post-pubertally ovariectomized and hysterectomized chimpanzees were used. L (dominant over N) was used as an uninjected control and 20 critical tests were done per day, each consisting in placing one cup in front of the cage and dropping in a peanut in view of the animals. The number of times each animal secured the peanut was counted. To avoid frustration on the part of the subordinate animal and test food motivation these were alternated with tests in which 2 cups were used; 4 sets of tests were done during the control and hormone administration periods.

Scores for L and N for the pre-injection period were 19 and 1 respectively (statistically significant; $P=0{\cdot}001$). N was injected with 2 mg. per day of α-oestradiol and tested when maximum swelling had been produced. Results were L 6 and N 14. Although this result was on the border-line of significance, observation showed that N was the dominant animal; the result was due to the high score obtained by L in the first test owing to N's slowness. Twelve days after stopping the injections the animals returned to their preinjection status (L 19·5; N 0·5). The authors conclude that dominance seen during the oestrogen phase of the normal cycle is in fact due to increased oestrogen secretion. [Their results, however, would be more convincing if more animals had been tested, particularly as M, when in a state of maximum swelling as a result of oestrogen pellet implantation, still remained subordinate to L and N (scores being 80 for L and N and 0 for M). This fact is offered as evidence that the dominance shown by N was not the result of " privilege-granting ", as M would mate readily although remaining subordinate to L and N.]

Methyl testosterone (50 mg. per day) was injected for 8 days prior to testing L and N. The increase in dominance did not reach the height attained during oestrogen injections, neither animal having clear dominance over the other (L 11; N 9). Prolonging the injections for a further week gave no better results (L 12; N 8). The effect of testosterone was more prolonged, as L did not regain her dominance until 3 weeks after injections had been stopped.

The authors consider that the same physiological mechanism underlies androgen dominance in males and females, but the response to oestrogen differs owing to the difference in peripheral response in the two sexes. They suggest that the oedema produced in the female causes an irritation absent in male castrates given oestrogen. They review sexuality and dominance, and suggest that mating is not necessarily accompanied by increased submissiveness on the part of the female.
S. A. Simpson

1923. **Aetiology and Pathogenesis of Diabetes Insipidus in Children.** (Studio sull'eziopatogenesi del diabete insipido infantile)
B. Rondinini. *Clinica Pediatrica* [*Clin. Pediat.*] **28**, 225–242, Aug., 1946. 4 refs.

After listing the pathological processes which may affect the hypothalamus and pituitary, giving rise to diabetes insipidus, the author examines the records of the 23 cases of the disease which have occurred in the Paediatric Clinic, Bologna, since 1903. Psychic trauma, tuberculosis, neoplasm, encephalitis, and hereditary factors play no part in the series. Trauma was responsible for 2 cases, which followed head injuries. One of these cases was relieved by the cutting of adhesions round the optic chiasma a year after the accident; the other was shown on *x*-ray examination to have a small sella turcica with approximated clinoid processes. In 2 other cases said to have been caused by trauma the evidence was insufficient. Syphilis was present in 2 cases, but no evidence was found to show a relationship between syphilis and diabetes insipidus. A further case followed an unspecified febrile attack, with convulsions and paralysis of the lower limbs; 1 case appeared after measles, and another occurred after a two-day fever. One case followed an intestinal upset, and 1 occurred after suppurative parotitis and otitis media in a child both mentally and physically underdeveloped. The brother of this last patient developed symptoms of diabetes insipidus. Another case was associated with xanthomatosis, and 1 with benign granulomatosis. Nine of the cases had no apparent precipitating cause. One had a Fröhlich's syndrome in association, another showed a poorly developed sella turcica, and a third which came to necropsy had a large lesion of the pituitary, with old scarring and recent inflammation due to the fatal illness (typhoid with peritonitis). The onset 10 months previously had followed a momentary giddiness and loss of consciousness. The author states that 13 cases had evidence of compression of the pituitary or hypothalamus, and remarks that nearly all cases showed marked lack of physical development.

[This is a fact not stressed by other authors. The evidence for compression of the pituitary or hypothalamus is vague and inadequate.] *J. G. Jamieson*

Dermatology

1924. **A Study of the Enzyme Metabolism in the Skin.** (Über den Fermentstoffwechsel der Haut). I.
R. SCHUPPLI. *Dermatologica [Dermatologica, Basel]* **93**, 97–110, 1946. 3 figs., 14 refs.

The author modified the Willstätter–Waldschmitt–Leitz method for the determination of diastase by using as material small biopsy pieces, about 1 cm. by 0·5 cm., of skin and cutting them in thin slices on a freezing microtome. As the biopsy can easily be repeated, the ferment content in one individual can be followed up without difficulty. In this way the diastase content in human subjects and in various animals under normal and pathological metabolic conditions was determined. The amount of diastase was established by determining the maltose formed in a starch solution. It was found that in only very severe cases of phloridzin diabetes in animals did the skin diastase decrease, with a parallel rise in the diastase of the liver. Other severe metabolic disturbances such as hyperthyroidism, beriberi, and diabetes due to adrenaline did not produce any change in the diastase content of the skin. Diastase contents in men, rabbits, guinea-pigs, and rats are in the proportion of 1 : 5 : 10 : 10. The diastase content in the skin is not higher than that in the serum or the liver.
W. Freudenthal

1925. **Diminished Lacrimal Secretion, Dryness of the Mouth without Polydipsia, Loss of Teeth and of Hair (Sjögren's Syndrome).** (Diminution de la sécrétion lacrymale, sécheresse de la bouche sans polydipsie, chute des dents, des poils. Syndrome de Sjögren)
J. C. MUSSIO-FOURNIER and G. POUMEAU-DELILLE. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris [Bull. Soc. méd. Hôp. Paris]* **62**, 398–399, July 5 and 12, 1946. 3 refs.

A veterinary surgeon of 58 complained of various trophic disturbances which had appeared during the last 4 years. There was no notable previous illness; he was in good general health and of normal build. Lacrimal secretion decreased without apparent cause and in a few weeks his saliva dried up, making talking and eating very difficult. Sweating then ceased over the whole body except on the forehead, where it became more marked than previously; there was no response to pilocarpine. The hair of the head fell out in large patches, except for the beard, eyebrows, and lashes, and the body hair completely disappeared. The crowns of the teeth crumbled away, leaving the roots behind. Loss of ano-rectal secretion made defaecation very difficult. The nails were normal. Gastro-intestinal secretions remained unaltered. No abnormality was detected in the other systems. There were no signs of endocrine disturbance or of syphilis. This clinical picture approximates closely to the syndrome described by Sjögren in 1933, who reported kerato-conjunctivitis sicca occurring with xerostomia, dryness of skin, and loss of teeth. One of his patients also had achylia, and he stressed the frequent occurrence of polyarthritis and of previous recurrent attacks of parotitis. Various components of the syndrome have been described separately, but abnormal dryness of the ano-rectal region, alopecia areata with loss of body hair, abnormally fine pectoral skin, and this peculiar fragmentation of the teeth have not previously been associated with Sjögren's syndrome. The aetiology is unknown. Sjögren believes that it is associated with an infection, such as parotitis or polyarthritis. Fried and Goldzieher think it may be due to endocrine disturbance, one of their cases having responded to stilboestrol and progesterone. The syndrome frequently occurs in women about the menopause. The authors consider that the hypothalamus in involved. [The possibility of a primary abiotrophy of the ectoderm is not mentioned.] *E. G. Sita-Lumsden*

1926. **Chemical and Clinico-Experimental Investigations into the Combination of Mercury with Salicylic Acid in the Treatment of Skin Diseases.** (Chemische und klinisch-experimentelle Untersuchungen über die Kombination von Quecksilberpräzipitat mit Salizylsäure bei der Behandlung der Hautkrankheiten)
H. W. SIEMENS and E. SCHREIBER. *Dermatologica [Dermatologica, Basel]* **93**, 89–96, 1946. 3 refs.

Ointments containing more than 1% of corrosive sublimate irritate the skin; the addition of 10% of salicylic acid increases the irritating effect. Ointments containing either 10% acid. salicylic. or 10% hydrarg. ammon. do not irritate, but irritation is caused if the two substances are combined. In an acid. salicyl. cum hydrarg. ammon. ointment, mercury salicylate, salicylate of ammonia, oxide of mercury (intermediary), and sublimate are formed. Of these four substances only the last is found to irritate the skin. The amount of sublimate formed in ointments containing from 2·5 to 10% of acid. salicyl. and hydrarg. ammon. depends to a large extent on the excess of salicylic acid. At room temperature this transformation takes place very slowly, on the skin much more quickly—a month at room temperature equalling about 24 hours on the skin. Old ointments do not irritate the skin more than fresh ones, probably because the formation of sublimate has reached its saturation point. Petroleum jelly as an ointment base causes less irritation than water-free " eucerin ", water-containing " eucerin ", or lard. *W. Freudenthal*

1927. **Cutaneous Manifestations of Systemic Disease**
H. T. BEHRMAN and O. L. LEVIN. *Journal of the Mount Sinai Hospital [J. Mt Sinai Hosp.]* **13**, 257–270, Jan.–Feb., 1947. 11 figs.

1928. **Complications of Lichenoid Dermatitis. Glomerulonephritis and Severe Pigmentary Changes in the Exfoliative Stage of Lichenoid Dermatitis**
E. S. BERESTON and M. S. SASLAW. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **54**, 325–329, Sept., 1946. 2 figs., 11 refs.

A case of lichenoid dermatitis occurring in a 31-year-old white officer is described. He was serving in New Guinea and had been taking 0·2 g. of quinacrine hydrochloride (mepacrine) daily for 5 months before he first noticed peeling of the skin of his hands with underlying redness. Within a few weeks the eruption became generalized and violaceous in colour; later all the skin began to ooze fluid and he was admitted to hospital in New Guinea on June 29, 1944. About this time the skin became scaly and the patient noticed that it was becoming darker; his urine was dark brown and his axillary and inguinal lymph nodes were swollen and tender. He was transferred to the United States and admitted to hospital under the care of the authors in September, 1944. He then had a generalized exfoliative dermatitis, and the whole of the skin was a dark coffee-brown colour. The inguinal, axillary, and cervical lymph nodes were enlarged, discrete, and firm, the liver and spleen were palpable, and there was a fever with a maximum temperature of 102·6° F. (39·2° C.) for 6 days; the sedimentation rate was 80 mm. per hour, haemoglobin 58%, red blood cells 2,810,000 per c.mm., and white cells 13,100 per c.mm. Red blood cells and albumin were present in the urine. Radiographs of the chest were normal and the blood nitrogen and non-protein nitrogen were 20 and 36·3 mg. per 100 ml. respectively.

The patient was given 100,000 units of penicillin intramuscularly daily for 5 days, and within 48 hours of the first injection the temperature became normal and remained so; he also had two blood transfusions for his anaemia; a high-vitamin high-calorie diet; ferrous sulphate orally; colloidal baths; boric acid compresses to the moist areas, and boric acid ointment to all the other areas. The condition steadily improved, but granular and pus casts were present in the urine in addition to the red blood cells and albumin after the first week, and by the end of October red cells were still present. After 5 months the patient was quite well apart from irregular areas of pigmentation scattered over his body.

Glomerulonephritis is unusual in either lichen planus or exfoliative dermatitis, and the role of quinacrine hydrochloride as a possible cause is mentioned.

H. R. Vickers

1929. **Dermatitis due to Quinacrine Hydrochloride**
F. T. BECKER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **54**, 338–344, Sept., 1946. 11 refs.

A short review of the types of eruption seen in soldiers returning to the United States from the South-west Pacific, where they had been receiving quinacrine hydrochloride (mepacrine) for suppressive antimalarial therapy, is followed by the description of 2 cases. Both these patients had recovered from a dermatosis, and both developed malaria when on leave in the United States. Administration of quinacrine hydrochloride for treatment of this resulted in a recurrence of the original dermatosis within 24 hours. In the first case the eruption was of the urticarial or fixed type of reaction, and in the second of the vesicular–bullous–eczematoid type. In both cases patch-testing to quinacrine hydrochloride was negative. The author concludes that quinacrine hydrochloride is responsible for a certain number of cutaneous reactions, but points out that such hypersensitivity to the drug is very infrequent and in no way reflects on its usefulness in the treatment of malaria.

H. R. Vickers

1930. **Relation of Quinacrine Hydrochloride to Lichenoid Dermatitis (Atypical Lichen Planus)**
J. M. BAZEMORE, H. H. JOHNSON, E. R. SWANSON, and J. M. HAYMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **54**, 308–324, Sept., 1946. 2 figs., 9 refs.

This is a report of an exhaustive attempt to find the course and best method of treatment of " atypical lichen planus ", with particular reference to the aetiological role of long-continued use of quinacrine hydrochloride (mepacrine). The two basic skin lesions—those which are raised above the surrounding skin and those which are not—are described in detail and the authors then discuss their experience of 400 patients, 314 of whom were studied in detail.

[It is impossible in the scope of an abstract to summarize the results of the many investigations. It is shown that prolonged ingestion of relatively large quantities of quinacrine hydrochloride is an important aetiological factor in the production of atypical lichen planus, but those interested are advised to consult the original paper.]

H. R. Vickers

1931. **The Penetration of Anti-gas Ointments into Skin**
H. CULLUMBINE and H. F. LIDDELL. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm.*] **58**, 294–297, Nov.–Dec., 1946.

Histochemically there is evidence that the active agents of anti-gas ointments do penetrate the skin. However, there is no sign of any available chlorine in the inuncted skin. The watery base of anti-gas ointment No. 2 penetrates better than the fatty base of anti-gas ointment No. 6.—[Authors' summary.]

1932. ***In Vitro* Fungistasis by a Bacterium (*Bacillus subtilis* var. XG and XY)**
G. M. LEWIS, M. E. HOPPER, and S. SHULTZ. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **54**, 300–307, Sept., 1946. 2 figs., 5 refs.

In 1928 Chambers and Weidman isolated bacteria, later identified as *Bacillus subtilis*, from apparently normal interdigital spaces of the feet of 4 subjects. This organism, when mixed with *Trichophyton gypseum* and cultured, completely inhibited fungous growth. The authors repeated this work, inoculating three different

strains of *B. subtilis* on to agar plates already heavily seeded with spores of *T. gypseum*. None of these inoculations inhibited fungous growth, but on one plate inhibition was seen round the small colony of a contaminant, and this colony was found to consist of a grey growth (named by the authors *Bacillus XG*) and a yellow growth (*Bacillus XY*), which later were shown to belong to the group of *B. subtilis*. *Bacillus XG* inhibited the growth of more pathogenic fungi than *Bacillus XY*, but the latter restrained the growth of certain bacteria. Fungi and bacteria inhibited by *Bacillus XG* are: *T. gypseum*, *T. purpureum*, *T. crateriforme*, *Microsporon audouini*, *M. lanosum*, *M. fulvum*, *Monilia albicans*, *Sporotrichum schenki*, *Aspergillus niger*, *A. nidulans*, *Penicillium notatum*, *Fusarium*, *Scopulariopsis*, *Hormodendron olivaceum*, *Alternaria*, *Chaetomium*, *Mycoderma*, *Acladium*, *Trichoderma*, *Torula* (pink), *Pneumococcus*, *B. subtilis*, *Streptococcus haemolyticus* (C.203).

The filtrate of *Bacillus XG* produces haemolysis of the red blood cells of the rabbit in dilution up to 1 in 640 and human red cells up to 1 in 320. This effect is reduced slightly by heating at 65° C. for 1 hour, and is greatly reduced by heating at 100° C. for 1 hour; but although the fungistatic property is not affected by heating at 65° C. it is destroyed by heating at 100° C. for 1 hour. Preliminary studies show that for inhibitory material to be present in the filtrate the presence of dextrose is necessary in the medium. *H. R. Vickers*

1933. **Kerion Celsi due to Infection with *Achorion schoenleini*.** [In English]
S. KAPLAN and F. RAUBITSCHEK. *Dermatologica* [*Dermatologica, Basel*] **93**, 110–112, 1946. 1 fig., 3 refs.

This is the fourth case of its kind described in the literature. Clinically it resembled an agminate folliculitis with a flat configuration, in contrast to the more globular infiltration seen in kerion caused by *Trichophyton mentagraphytes*. Histologically it was identical with the ordinary type of kerion. *W. Freudenthal*

1934. **Treatment of Lupus Vulgaris with Large Doses of Vitamin D_2.** (Behandeling van lupus vulgaris met hooge doses vitamine D_2)
W. J. HOHMANN and G. W. BEENING. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **91**, 78–82, Jan. 11, 1947. 14 figs., 10 refs.

The authors used the treatment of lupus introduced by Dowling, who gave 1 to 3 calciferol tablets daily, each containing 50,000 I.U. of vitamin D_2, for 6 to 12 months. The advantages were that treatment was ambulatory, there were no unpleasant local applications, improvement was rapid with good psychological effect, and scar formation was small. The authors treated 87 patients, 31 men and 56 women, with "dohyfral" tablets (30,000 I.U. vitamin D_2). The patients received one tablet thrice daily for the first week, then one tablet five times daily for 3 months. After this one tablet thrice daily was again given, and later one tablet daily. Most of the cases were chronic and had hitherto proved intractable. In some cases the disease had become quiescent but had never healed. The condition of 14 male and 20 female patients had formerly deteriorated in spite of regular treatment and good feeding. With the administration of vitamin D_2 all 87 improved. Lupus tumidus became flat and healed with small scars; in lupus ulcerosus the ulcers closed quickly. The skin regained its suppleness and the mucous membranes showed similar effects. No local treatment was necessary. In severely affected patients there was an improvement amounting to clinical cure, but the pathologists found that in fact tubercles persisted and nodules did not calcify.

Very large doses of vitamin D_2 seem to be well tolerated if the preparation is pure. Harmful effects are rare. American authors demand careful observation of the patients. Toxic effects, according to them, depend on many factors, and these change often, even in the same patient. Calcium determinations are misleading and unnecessary; more important are the patient's symptoms: dizziness, nausea, headaches, slight stomach complaints, thirst, anorexia, sweat, and fatigue. Sometimes the calcium level in the blood was high at first and became normal with the taking of the vitamin preparation. The serum calcium level can be easily determined by examining the urine with Sulkowitch's reagent: no precipitate means a low calcium level, white turbidity is normal, and a milk-like precipitate indicates increased calcium in the specimen. Symptoms of intolerance arising from a large dose disappear when treatment is discontinued for a short period; if treatment is resumed with a lower dose they do not return when the dose is raised again. The diet should be low in fat; calcium administration is unnecessary. It is possible that smaller doses of the vitamin may have the same good effect.

[The photographs of patients are a striking justification of the claims made in the text.] *B. Baneth*

1935. **The Treatment of Lupus of the Palate.** [In English]
B. J. RIENKS. *Acta Dermato-Venereologica* [*Acta derm.-venereol., Stockh.*] **27**, 39–44, June, 1946. 4 refs.

The general and local treatment of lupus of the palate is reviewed. General treatment includes rest in bed, a diet rich in calories and vitamins, gold or bismuth injections, and autohaemotherapy. Local treatments used were the application of lactic acid (10 to 50%), hydrogen peroxide, and "lenigallol" paste. This latter was applied to the palate by means of a prosthesis. Six patients were given *x*-ray therapy, with a Philips contact *x*-ray apparatus. Varying doses were used but no effective dosage has been worked out. In 5 cases the lupus cleared completely, and the other case improved. *F. H. Cross*

1936. **Treatment of the Dermatophytid**
A. A. HOLBROOK. *Urologic and Cutaneous Review* [*Urol. cutan. Rev.*] **5**, 542–545, Sept., 1946.

The treatment of dermatophytide pompholyx of hands and feet in troops in the South-West Pacific area is discussed. Attempted eradication of the infection by

fungicides and treatment of the condition along the lines used in eczema were rarely followed by subsidence of the symptoms. Of 26 cases treated with liquor arsenicalis internally, only 1 did not regress completely. The dosage recommended was 10 drops thrice daily, increased to 15 drops thrice daily and then reduced again to 10 drops thrice daily. Gastro-intestinal upsets and ocular discomfort were occasional side-effects. The author's conclusion is that Fowler's solution given by mouth tends to suppress the eruption due to the dermatophytides. *Geoffrey A. Hodgson*

1937. **Control of Ringworm of the Scalp among School Children in Hagerstown, Md., 1944–1945**
L. SCHWARTZ, S. M. PECK, I. BOTVINICK, A. L. LEIBOVITZ, and E. S. FRASIER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 58–62, Sept. 14 1946.

From August, 1944, to November, 1945, as ringworm of the scalp had reached epidemic proportions, 8,657 children in Hagerstown were examined by the Wood light for the presence of the disease. Some 565 children were infected, all positive cases were examined microscopically and culturally, and in all but 8 cases *Microsporon audouini* was identified; the disease was found to be six times more common in boys than in girls. The "clippers area" was the site of infection in 65%, this and other areas in 31%, and the crown alone in 4%, so that in 96% the "clippers area" was involved. This suggested that infection might have been through clippers, and investigations at hairdressers' establishments confirmed this supposition. Combs and brushes containing infected hairs played only a minor part. Spread from other sources was very much rarer—fewer than 10% of cases were traced to home contacts, and when such cases occurred it was found that the children had nearly always slept together or used the same comb. The children were allowed to attend school, but had to have their hair closely cropped, to wear skull-caps, and to submit to local application. As the number of cases was so large *x*-ray epilations were not feasible, and control of the epidemic had to be confined to general measures and the sterilization of barbers' implements. Clippers could be sterilized without damage by working them for 10 seconds while immersed in petroleum oil (boiling-point 150° to 200° C.) at 100° C., by boiling them for 3 minutes in a 2% saponated solution of cresol, or by immersing them in a 10% solution of this in the cold for 15 minutes. These methods of control led to a drop in incidence from 9·3% (October, 1944) to 0·9% (December), 0·5% (March, 1945), and 0·2% (September, 1945).

Of the 565 children infected, 493 were treated at public health centres; 48 were cured by manual epilation and one or two topical applications; and 274 by applications alone, while 126 stopped treatment before being pronounced cured; 45 were still under treatment when the study period ended, but later 38 of these were found to be cured. If the 126 who stopped treatment are excluded the percentage of cures was 98. Seventeen medicaments were used, though a child might be treated with only one or two of these. Salicylanilide, 5% in carbowax 1500 and a saturated solution of copper undecylenate in carbowax 1500 were found to be the most effective remedies. *Geoffrey Duckworth*

1938. **Erythema Multiforme. With Special Emphasis on Postvaccinal Erythema**
M. H. SCHWARTZ and H. D. BRAINERD. *Journal of Pediatrics* [*J. Pediat.*] **29**, 512–517, Oct., 1946. 11 refs.

The authors record 6 cases of erythema multiforme. Three of these are attributed to vaccination against smallpox, one to rheumatic fever, one to injection of horse serum, and one to no discernible cause. The rashes that may occur after vaccination and the rarity of this condition are pointed out. The authors are of the opinion that involvement of the mucous membrane, the so-called Stevens-Johnson syndrome, which occurred in 4 cases, should not be considered as a separate condition; and that this greyish membrane in the mouth, and conjunctival haemorrhage and engorgement when they occur, are so typical as to be pathognomonic. Three of the cases had a diffuse pneumonitis.

It is concluded that erythema multiforme is a rare complication of vaccination against smallpox, that the mouth lesion is pathognomonic, and that pneumonitis is frequent; because of an allergic history in 3 of the cases it is suggested that erythema multiforme represents an allergic reaction.

[It would be unwise to base any conclusion, except that of the rarity of this condition as a sequel to vaccination, upon so few cases.] *R. E. Bonham-Carter*

1939. **Epidermolysis Bullosa Hereditaria**
M. M. ROBINSON. *Urologic and Cutaneous Review* [*Urol. cutan. Rev.*] **5**, 545–561, Sept., 1946. 23 figs., 69 refs.

A comprehensive review is given of the literature on epidermolysis bullosa; it should be read in its entirety. The author believes that all cases are caused essentially by some hereditary derangement of the germ-plasm. He describes 25 cases, 18 of which occurred in three families. Inheritance occurs by heterozygous dominant and recessive genetic transfer. Study of family history pedigrees confirms that there is a hereditary factor. Dominant genes produce mild types of the disease, while recessive ones give rise to other developmental stigmata and ectodermal abnormalities. The absence of elastic tissue fibrils in the basal layer and the fragmentation of deeper elastic tissue are important factors in bulla formation. A hereditary hyperreaction of the superficial blood vessels to trauma may cause them to be more permeable.

The author makes a plea for considering all forms of the disease not as entities but as parts of a symptom-complex, or genodermatosis. The complex would include all types of epidermolysis—simplex, dystrophic, and acquired (re-named 'tarda'), and other diseases such as familial benign pemphigus and dyskeratosis vesicularis hereditaria. *Geoffrey A. Hodgson*

Venereal Diseases

1940. **A Bacteriologic Study of the Resistance of Organisms Isolated from Cases of Non-specific Urethritis to Three Chemotherapeutic Agents**
A. M. WECKSTEIN and S. H. RASMUSSEN. *Military Surgeon* [*Mil. Surg.*] **99**, 312–316, Oct., 1946. 5 refs.

In this study the authors set out to determine the nature of the organisms present in non-gonococcal urethral discharges and to ascertain to what extent these organisms are resistant to the usual chemotherapeutic agents. Cultures of the prostatic fluid in 100 cases of non-specific urethritis were collected by means of a swab passed 2 cm. into the urethra after preliminary cleansing of the glans with green soap followed by 70% alcohol. The inoculated plates of whole blood, haemolysed blood plasma, and agar were incubated under partial carbon dioxide tension for 24 hours. The organisms grown were isolated in pure culture on blood-agar slopes, and, when adequate growth had occurred after further incubation, were emulsified in 2 ml. of sterile normal saline added to the culture tube. Of this suspension 0·1 ml. was then added to 2 ml. of nutrient broth in test tubes containing respectively, penicillin (13·2 units), neoarsphenamine (1 in 10,000), and sulphadiazine (1, 5, 25, 125 mg. per 100 ml.). A seventh tube without any inhibitory substance was inoculated as a control. These tubes were incubated for 24 hours and the resultant organisms were there replanted and incubated for a further 24 hours on enriched blood-agar plates.

The results of this investigation are shown in a table, study of which discloses that a haemolytic *Staphylococcus albus* is present in over 68% of the cases, other organisms being present in lesser proportions. Sixty-five per cent. of all the strains were resistant to penicillin, 69·5% to neoarsphenamine, and 95% to as much as 125 mg. per 100 ml. of sulphadiazine. It is stated that though there was no controlled follow-up the doctors treating the patients formed the impression that their results agreed with the authors' *in vitro* findings.

[It would be interesting to know to what extent the organisms isolated in these cases are to be found in the urinary meati of apparently healthy individuals.]

G. L. M. McElligott

1941. **Penicillin in the Treatment of Lymphogranuloma Inguinale**
N. V. RAO. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **22**, 135, Sept., 1946.

It is generally believed that penicillin is ineffective in the treatment of lymphogranuloma inguinale (lymphogranuloma venereum) but during preliminary observations on patients with primary or secondary syphilis and co-incident lymphogranuloma venereum, the author observed that the lymphogranuloma bubo had subsided by the time the patient had received 2,000,000 units of penicillin for the syphilis. The progress of the lymphogranuloma lesions was arrested, and definite signs of healing of the sinuses which had formed in some cases were observed. In further trials with penicillin in cases of syphilis and co-incident lymphogranuloma, the chancre healed and the rash faded; the bubo also responded well in each case. The number of cases treated is not given. A case of lymphogranuloma venereum resistant to sulphanilamide and to " urea stibamine " is reported, in which cure was effected with 100 injections (20,000 units each, 3-hourly) of penicillin.

T. Anwyl-Davies

SYPHILIS

1942. **Syphilitic Amyotrophy. Clinical-pathological Report of a Case Complicating Tabes Dorsalis**
B. W. LICHTENSTEIN and J. A. LUHAN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **5**, 321–332, Oct., 1946. 4 figs., 24 refs.

In a clinical sense the term syphilitic amyotrophy designates an atrophy of muscles resulting from syphilitic involvement of the nervous system. The anatomical basis may be of vascular origin, as in syphilis of the spinal arteries and their branches; of medullary origin, as in syphilitic myelitis or gumma of the spinal cord; of meningeal origin as in syphilitic leptomeningitis or pachymeningitis; and of radicular or neuritic origin. Not infrequently these histopathological states are present in combination, and in many instances syphilitic amyotrophy is found in association with tabes dorsalis and general paresis. In the case reported by Lichenstein and Luhan, in addition to the typical lesions of tabes, the cord showed evidence of a chronic meningomyelitis. In the cervical enlargement the loss of motor nerve cells was pronounced. No spirochaetes were found.

R. M. Stewart

1943. **Penicillin in the Treatment of Syphilis in Children**
J. YAMPOLSKY and A. HEYMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 368–371, Oct. 19, 1946. 3 refs.

The results are reported of treatment with penicillin in 54 congenital syphilitics and in 7 children with acquired primary and secondary syphilis. During 20 months the authors treated with penicillin alone 32 children with infantile congenital syphilis; 22 were watched for 12 to 20 months, 7 for 4 to 8 months, while the remaining 3 died from causes unconnected with the treatment. At first 40,000 to 50,000 units of sodium penicillin per kilo of body weight was given intramuscularly every 3 hours for a total of 60 doses in 7½ days, but when failures were observed the dosage was raised to 60,000 and 70,000 units. An immediate clinical response, including the healing of mucosal and cutaneous lesions, and improvement in osseous lesions, occurred in all patients. The

serological tests became negative in 18 cases, decreased in titre in 5, but remained unchanged in 6. Harmless Herxheimer elevations of temperature occurred in 50% of cases; no other reactions were seen. Penicillin was effective in only 1 case of interstitial keratitis; 3 improved and 5 were unsatisfactory. No benefit resulted when penicillin was instilled locally. Three children with Clutton's joints (symmetrical hydrarthrosis) and 2 with juvenile general paralysis failed to respond clinically. In late congenital asymptomatic neurosyphilis the cell count and protein content of the cerebrospinal fluid were reduced rapidly in 6 patients, but became normal within 12 months in only 4 of these. The Wassermann reaction, however, has remained positive in every case. In one severe case of eighth-nerve deafness no change was detected, but hearing was improved in a milder case. The lesions in the 7 cases of acquired syphilis healed promptly and the spirochaetes disappeared rapidly, but in only 2 did the serological reactions become positive.

This study suggests that infantile congenital syphilis and early neurosyphilis respond well, and that interstitial keratitis, Clutton's joints, eighth-nerve deafness, and juvenile general paralysis are refractory; that is to say, that only a poor response is to be expected in the late manifestations of the disease.

[The authors state that they are now using 100,000 units of penicillin every 3 hours for the longer period of 10 days. General experience suggests that the doses of penicillin employed were too small, and that much better results would be obtained if the dosage is raised to at least 100,000 units per kilo of body weight, and if penicillin is combined with bismuth and arsenical therapy.]

T. Anwyl-Davies

1944. **The Treatment of Experimental Syphilis with Penicillin**

C. M. CARPENTER, R. A. BOAK, and L. M. JACOBS. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **46**, 2150–2153, Oct. 1, 1946.

This important report from the University of Rochester, N.Y., describes a prolonged series of experiments to assess the therapeutic efficacy of sodium penicillin and of penicillin fractions F, G, and X upon syphilitic infection in rabbits. The authors found that penicillin is capable of curing 100% of syphilitic rabbits if it is given over a sufficiently prolonged period, and that this " time factor " appears to be more important than heavy dosage.

Experimental syphilis was produced with the Nichols strain of *Treponema pallidum* in male rabbits weighing from 2·5 to 3·5 kilo. Their testes with well-developed syphilitic lesions are titrated with sufficient 0·85% sodium chloride to obtain a 20% tissue suspension. After motile spirochaetes were demonstrated by darkfield examination, 0·5 ml. of the suspension was injected into each testis of a normal rabbit: usually groups of 10 animals were inoculated. Intramuscular penicillin therapy was initiated 6 weeks later when typical chancres containing *T. pallidum* were present. When a treatment schedule was completed, the animals were isolated and inspected bi-weekly for 6 months. If syphilitic lesions containing *T. pallidum* recurred the result was recorded as a failure. If no lesions developed during this period the rabbit was killed and the testes and lymph nodes were removed. A triturated suspension of these tissues was made by adding 1·5 ml. of a mixture of equal parts of rabbit serum and physiological saline to the testes and lymph nodes separately. One ml. of the testicular suspension was injected into the right testis, and the lymphatic suspension was injected into the left testis, of a serum-negative rabbit. The Kahn and Wassermann tests were carried out on these " test for cure " animals at monthly intervals for 6 months. When neither lesions nor a positive blood reaction developed the originally treated rabbit was considered cured.

Six schedules of penicillin treatment were tested. (1) Single injections of sodium penicillin ranging from 2,000 to 50,000 units per kilo body weight were ineffective. (2) Two doses of 8,000 units each at a 3-hour interval were ineffective. (3) and (4) Up to 16,000 units per kilo of body weight at hourly intervals for as long as 16 hours also failed to cure. (5) Two daily injections at 8-hour intervals for 16 days; 10, 0, 0, 90, 100, and 100% respectively of the animals treated with 250, 500, 1,000, 2,000, 4,000, and 8,000 units per kilo were cured. (6) The therapeutic value of penicillin fractions F, G, and X was compared; one injection every 4 hours for 4 days showed that fraction G was far more effective than fractions F or X. Fraction G cured, respectively, 0, 40, 70, 100, 90, and 90% of rabbits treated with 500, 1,000, 2,000, 4,000, 8,000, and 16,000 units per kilo. Fraction X was much less effective than fraction F; 50% of the rabbits treated with 16,000 units of fraction X per kilo of body weight relapsed clinically as against 30% treated with the same dosage of fraction F. A comparison of these schedules demonstrates that a single injection of as much as 50,000 units per kilo, equivalent to 3,500,000 units for a man weighing 70 kilo, fails to cure. Also, 16,000 units per kilo, equivalent to 1,200,000 units in human syphilis, injected at the rate of 1,000 units an hour for 16 hours, was ineffective, but fewer clinical relapses occurred than when more than three times as much penicillin was given as a single dose. This prolonged " time factor " seems to be more important in effecting a cure than larger doses of penicillin.

[Study of these results reveals their importance and value. They indicate that to achieve success, the penicillin fraction, the dose, the intervals at which the drug is given, and the duration of treatment, must all be carefully considered.] *T. Anwyl-Davies*

1945. **Neurosyphilitic Patients Treated with Penicillin. Probable Herxheimer Reactions**

H. A. TUCKER and R. C. V. ROBINSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **132**, 281–283, Oct. 5, 1946. 9 refs.

Since penicillin will be used increasingly in the treatment of neurosyphilis the authors believe that it is important to record two examples of probable Herxheimer reaction in such cases. The first patient was a white woman, aged 32, with clinical evidence of dementia paralytica. This diagnosis was confirmed by cerebro-

spinal fluid examination. Symptoms had been present for 10 months and included aphasia and right-sided hemiparesis, suggesting softening of the left internal capsule adjacent to Broca's area. Treatment comprised 50,000 Oxford units of sodium penicillin given intramuscularly in normal saline every 3 hours to a total of 10,000,000 units. After 30 hours the patient's rectal temperature had risen to 100·8° F. (38·3° C.), and at 42 hours a prolonged series of clonic convulsions began, affecting the right arm and leg and the right side of the face. Swallowing was impaired initially and plantar responses were extensor but there was no incontinence. In spite of anticonvulsant drugs the convulsions continued for 15 days, penicillin being given all the time. Eight days later the patient left hospital, there being considerable improvement in the dementia paralytica. Clinical improvement continued for the 6 months during which the patient was followed up.

The second patient, a negro aged 30 years, was asymptomatic but in the cerebrospinal fluid there were 53 cells per c.mm., with 142 mg. of protein per 100 ml., a colloidal mastic curve of 5555432100, and a Wassermann reaction positive in 0·05 ml. of fluid. Infection had occurred 3 years previously and treatment had been grossly inadequate. Penicillin therapy similar to that used in Case 1 was started. After 8 hours the patient had a rectal temperature of 102·6° F. (39·3° C.) which returned to normal spontaneously. After 24 hours he was restless, but otherwise normal, until 30 hours from the beginning of the penicillin therapy when he was found on the floor, moaning and throwing his body from side to side. Vomiting, incontinence, disorientation, and restlessness were prominent features. Meningeal irritation was marked and plantar responses were extensor. Lumbar puncture gave a clear, sterile fluid under normal pressure but the pleocytosis had increased to 277 cells per c.mm., of which 52% were polymorphonuclear cells. The rectal temperature rose to 104·8° F. (40·3° C.). Sedation was required for 3 days after which the patient recovered.

The authors believe that the reactions observed in these 2 cases were probably examples of the Jarisch-Herxheimer phenomenon because of their onset within 48 hours of the start of penicillin therapy and because of the associated pyrexia. While they accept the published reports showing that penicillin may cause irritative phenomena when given intracisternally, intraventricularly, intrathecally, or by direct local application of concentrated solutions to the cerebral cortex, they do not consider that the convulsions in their own patients were due to a direct irritative action on the nervous system since: (*a*) only insignificant amounts of penicillin have been demonstrated in the spinal fluid after massive intramuscular doses; and (*b*) the convulsions ceased although penicillin was continued throughout in full doses. The penicillin used contained penicillin G, F, and K in unknown proportions, K probably being the predominant fraction, and the authors speculate whether the differences, if any, between the various penicillin fractions are concerned in the production of irritative reactions in the nervous system. They conclude that the potential gravity of the neurological reactions reported deserves wider recognition.

[They might have gone further and emphasized the additional dangers of severe Herxheimer reactions affecting the cardiovascular system since cardiovascular syphilis is present in about 15% of neurosyphilitic patients.]

S. M. Laird

1946. **Value of Hoffmann's Lymph-node Puncture in the Diagnosis of Early Syphilis.** (Der diagnostische Wert der Erich Hoffmannschen Lymphdrüsenpunktion bei frischer Syphilis)

H. WILDE. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **1**, 93–94, Aug. 15, 1946. 12 refs.

Erich Hoffmann first demonstrated in 1905 that lymph-node puncture is a valuable aid to the diagnosis of syphilis in its earliest stages. Positive results by this method may establish a diagnosis weeks before serum reactions become positive. *Treponema pallidum* can be found by lymph-node puncture in a very high percentage of cases of early syphilis—100% according to Photinos; over 90% according to Habermann and Mauelshagen. Specimens are collected in the following manner. After cleansing the skin a wide-bore needle on a tight-fitting 10-ml. syringe is plunged into the lymph-node substance. The lymph node is fixed between thumb and forefinger of the other hand and gently massaged while suction is applied continuously by the syringe and the needle is moved about. The needle is then withdrawn and its contents expressed on to a slide and prepared for dark-ground examination.

The author found *T. pallidum* by this method in 84 out of 100 cases of proved primary syphilis. In 34 cases a positive result was obtained at the first test, in 23 at the second, in 11 at the third, in 8 at the fourth, in 4 at the fifth, in 1 at the sixth, in 2 at the seventh, and in 1 at the eighth test. In 78 cases with phimosis due to inflammatory conditions *T. pallidum* was discovered in 49. Further investigation of the 29 negative cases, after dorsal slit, showed them to consist of 8 primary chancres, 12 soft sores, and 9 non-specific ulcers. The method is very useful when *T. pallidum* cannot be found in sores which have been treated locally with antiseptics. Generally repeated tests of serum from typical syphilitic chancres fail to reveal *T. pallidum*, and in such cases puncture of a lymph node frequently establishes the diagnosis. In secondary syphilis positive tests were obtained in this manner in 44 of 63 cases—a smaller percentage of positives than in the primary stage.

James Marshall

1947. **The Systemic Treatment of 227 Cases of Arsenic Poisoning (Encephalitis, Dermatitis, Blood Dyscrasias, Jaundice, Fever) with 2,3-Dimercaptopropanol (BAL)**

H. EAGLE and H. J. MAGNUSON. *American Journal of Syphilis, Gonorrhea, and Venereal Diseases* [*Amer. J. Syph.*] **30**, 420–441, Sept., 1946. 2 figs., 19 refs.

This paper deals with the systemic treatment of 227 patients who showed signs and symptoms of arsenic poisoning during antisyphilitic therapy. The effect of "BAL" on arsenical encephalitis, dermatitis, blood dyscrasias, jaundice, and fever is described. A few cases

of accidental administration of overdoses are mentioned, and a routine to be followed in cases of arsenical poisoning is described. Observations on the urinary arsenic level after BAL are recorded. The drug was given intramuscularly in doses of 2·5 to 3 mg. per kilo of body weight repeated at 4-hourly intervals. The injection solution was made up of 10% BAL in peanut oil, containing 20% benzyl benzoate. The only important local reaction was pain at the site of injection. No serious systemic signs of BAL poisoning were encountered, but the symptomatology of larger doses (4 to 5 mg. per kilo) is described. In order of decreasing frequency, symptoms include nausea, vomiting, headache, a burning sensation in the lips, mouth, throat, and eyes, sometimes associated with lacrimation, salivation, and rhinorrhoea, generalized muscular aches, burning and tingling of the extremities, sweating of forehead and hands, pain in the teeth, a constricted feeling in the chest, and a feeling of anxiety.

The reports of the separate conditions treated were as follows:

Arsenical Encephalitis.—Fifty-five patients were treated, of whom 12 died. All the deaths were among the severely ill group. Fifteen patients with relatively mild symptoms (hyperexcitability, tremor, disorientation, hallucinations, and semistupor, but not convulsions) all recovered within 1 to 4 days. In those comatose or having convulsions results depended on the time since onset of symptoms when treatment was started. Thus, in the first 24 hours 14 out of 24 severely ill patients died, while in the next 24 hours 5 out of 9 died.

Arsenical Dermatitis.—Reports are given of 88 patients, of whom 51 had an exfoliative dermatitis. The remaining 37 were classified as mild, and showed a papular itching eruption but little or no exfoliation at the time treatment was begun. Results in the mild cases were good: 35 of 37 were cured within 5 to 6 days; the other 2 cases did not respond to BAL in the doses used. The severe cases took longer to respond, and had all been in progress for from 3 to 69 days before BAL was given. Of these patients 41 made a good recovery within 15 days. Ten patients failed to respond, of whom 3 died and 2 were inadequately treated. Several practical points should be emphasized: (1) Of the total number of patients treated with BAL by injection 5 developed abscess or cellulitis at the site of injection; this seems to be the result of injection through an infected area. (2) In the severe cases the oedema and inflammatory response of the skin subsided rapidly (within 3 days) but the exfoliative process often progressed, and even accelerated after the commencement of BAL. (3) Relapses may occur and should be treated with a further course of BAL. (4) Adequate treatment is essential and should be started as early as possible. (5) The time course of cure is longer than with arsenical encephalopathy, the average time being 13 days.

Blood Disorders following Arsenicals.—Eleven patients with agranulocytosis and 3 patients with aplastic anaemia are considered. Of the first group, 10 recovered promptly on the administration of BAL. Polymorphonuclear cells increased disproportionately to a greater extent than the other white cells of the blood. The remaining patient died. The white cell counts of these patients varied from 600 to 3,800 per c.mm. (polymorphs 0 to 30% of total). Most had received their last injection 1 day before the onset of the condition and 3 days before BAL was started. The value of these results is vitiated by the multiple forms of treatment, which included pentnucleotide and blood transfusion. Of the 3 patients with aplastic anaemia, none received any benefit from BAL as indicated by the haemopoietic response. Two of the patients died. The complication was present for 2 to 3 weeks before BAL was started.

Arsenical "Hepatitis".—Fourteen cases are reported, but the results are quite inconclusive. Five patients showed some symptomatic improvement after BAL; in 3 of these the blood bilirubin showed a prompt fall. Of the remaining patients 7 showed no response; the other 2 showed a debatable one.

Febrile Reactions.—Since this complication clears up in any case, it is difficult to evaluate results. BAL injection was attended by a rapid fall in temperature and subsidence of symptoms. There are 44 patients reported, of whom 36 had recovered in 3 days, and all were well within 8 days.

Accidental Poisoning from Massive Doses.—Four patients are considered, who received 0·6 g., 0·4 g., 0·6 g., and 1·2 g., respectively, of "mapharsen" at a single injection. All these showed immediate and alarming reactions. Three of them recovered promptly and without further complications after starting BAL injections. This treatment was begun within ½ to 2 hours, and 24 hours, respectively. The fourth patient received a dose equal to LD50 for rabbit and dog, and was inadequately treated with BAL. He died despite an initial favourable response.

Miscellaneous.—A 3-year-old child who received massive doses of sulpharsphenamine (900 mg. in 3 days) developed severe symptoms, and despite small doses of BAL died in 12 hours. Two patients with long-standing dermatoses resulting from the use of Fowler's solution showed no response to BAL. Four patients with amblyopia due to tryparsamide showed a favourable response, but this cannot be evaluated on the data presented. Further investigation is well worth while.

An increased urinary arsenic level was found after BAL treatment had been started in 11 patients with exfoliative dermatitis. In 1 patient who received 0·6 g. mapharsen at one injection in error it was found that 80 mg. of arsenic was excreted in the urine alone in the first 5 days. This corresponds to 260 mg. of mapharsen, or nearly half the total dose. The excretion of arsenic in the urine of several volunteers who inhaled small amounts of an arsenical smoke was also found to be increased after BAL.

As regards dosage, intramuscular injections of 2·5 to 3 mg. of BAL in peanut oil and benzyl benzoate per kilo of body weight at 4-hourly intervals are suggested, the patient receiving 500 to 700 mg. of BAL in the first 24 hours, and a total of 1,000 to 1,500 mg. over a period of 3 days to a week, as follows: For mild cases 2·5 mg. per kilo per injection; first 48 hours, four injections each day at 4-hourly intervals; thereafter one or two injections daily till recovery is complete. For severe cases 3 mg. per kilo per injection; injections should be made every 4 hours for the first 48 hours (twelve injections in all); after this, depending on response, the number of injections may be reduced to two daily till recovery is complete. *J. D. Judah*

1948. **Temperature Regulation Changes in Congenital Syphilis.** (Le alterazioni della termoregolazione nella silfilide congenita)

A. Bollettino. *Pediatria del Medico Pratico* [*Pediat. Med. prat.*] **19–21**, 331–340, Aug., 1946. 14 refs.

The author describes a case of "essential luetic fever" in a 3-months-old infant with congenital syphilis. The occurrence of essential luetic fever is rare and not accepted by all authors; its early diagnosis, however, is of obvious practical importance. According to Milian, pyrexia is present in 25% of cases of congenital syphilis, and the affected infants frequently show a marked thermic lability. Where secondary infection is absent the temperature does not usually rise above 38° C., apart

from the acute initial stage of the variety called " septic lues ". The fever in congenital syphilis characteristically precedes the manifestations from organic foci—for instance, those of osteochondritis, arthritis, hepatomegaly and splenomegaly, and lymph-node enlargement. The condition of the patient is influenced more by the nature of the organic lesion than by the temperature. Another frequent sign of congenital syphilis in the infant is an abnormally low temperature, or a disorder of the temperature regulation in which hyperthermy and hypothermy alternate. The latter is often refractory to mercury and responds only to arsphenamine preparations. In " essential syphilitic fever " there are no other signs of disease.

In the case described the parents were undergoing antisyphilitic treatment. When the child was 2 months old rises of temperature up to 38·5° C. were first noticed. As a lung infection was suspected, a sulphonamide preparation was prescribed. The temperature curve, however, assumed the character of a continuous fever, between 38·5° and 39·9° C. The nutritional condition, after a febrile phase of 1½ months, was only slightly affected; the skin was pale and dry, and the muscles hypotonic and hypotrophic. There was a diffuse distribution of small swollen lymph nodes, while the liver and spleen were enlarged with sharp margins and of hard consistency. The urine contained albumin ++ and some casts. Blood examination showed anaemia, lymphocytosis, and eosinophilia. The Wassermann test was positive. As regards diagnosis, acute or subacute infections of gastro-intestinal, pulmonary, or oral origin had first to be excluded. These were ruled out by the regular increase of weight, in spite of prolonged fever, in an artificially fed child. Typhoid fever was excluded by blood and serum examination. There was no clinical or radiographical sign of tuberculosis. The moderate degree of monocytosis excluded glandular fever, and in addition the infant did not show the other characteristics of this condition. *X*-ray examination showed no local syphilitic changes in the bones. During the first 2 weeks treatment consisted of mercury inunctions and a sulphonamide preparation orally; protein shock therapy was also used [names of preparations are not given]. In this period the condition of the kidneys improved rapidly (albumin and casts disappeared from the urine), and the size of the liver and spleen diminished progressively. The fever remained unaltered, but in spite of this the infant showed a regular increase in weight and improvement of nutrition in the third week. Treatment with neoarsphenamine injections was started while the mercury inunctions were continued. With the introduction of this treatment the fever terminated by crisis and the blood count became normal. The negative response to sulphonamide and protein therapy, the partial effect of the mercury treatment, and the striking change brought about by the arsenical injections are taken as proof of the essential syphilitic nature of the fever.

This " essential syphilitic fever " is regarded as an expression of syphilitic toxaemia together with either an organic hypersensitivity or a particularly virulent infection in an individual with low immunity.

Hilde Eisner

1949. **Preservatives for Syphilitic Serum with Special Reference to the Use of Merthiolate**

C. C. Croft and L. L. Smith. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **31**, 1101–1112, Oct., 1946. 13 refs.

When serological tests for syphilis are required it is preferable to send whole blood to the laboratory. Sometimes specimens are liable to long delay in transit with the risk of gross haemolysis and decomposition occurring. Under these conditions it is best for the sender to separate the serum himself and dispatch this to the laboratory; unfortunately, however, it is then common to receive specimens which are unsuitable for testing because of contamination. The authors have therefore investigated a number of antiseptics for their ability to preserve sera without affecting the results of serological tests. A total of 19 preservatives, including " merthiolate ", " sulpho-merthiolate ", 8-hydroxyquinoline, phenylmercuric borate, sulphanilamide, toluol, and sodium fluoride, were tested in suitable dilutions, a filtered pool of positive syphilitic sera being used. The mixtures were placed in non-sterile containers, and at intervals up to 17 days the standard and quantitative Kahn tests were performed; the presence or not of contamination was also noted. Only 9 of the 19 preservatives seemed promising and were investigated further; the others either failed to prevent contamination or reduced the titre in the Kahn tests. Later sodium fluoride was found to render a negative serum positive and its use was abandoned. In repeated tests, each extending up to 4 weeks, merthiolate gave the best results; sulphomerthiolate was almost equally effective. Phenylmercuric borate and nitrate (1 in 5,000), sulphanilamide (5 mg. per ml.), and toluol (0·06 ml. per 5 ml.) did not consistently prevent contamination; and 8-hydroxyquinoline sulphate (1 in 2,000) produced a precipitate in the serum.

Merthiolate was added to routine specimens of sera received for diagnosis, and the Kahn test was performed immediately and at weekly intervals for 3 weeks. To 81 positive and 12 negative sera 1 in 1,000 merthiolate was added; 200 positive and 23 negative sera were preserved with 1 in 2,500 merthiolate. Less than 4% of the sera containing 1 in 2,500 merthiolate showed a fall in titre with the Kahn test at the end of a week, and in only 7·3% was there a significant reduction in titre after 3 weeks; only 14 out of 223 sera became contamined. A concentration of 1 in 2,500 merthiolate was recommended, as 1 in 1,000 more often caused a reduction in titre. *D. G. ff. Edward*

1950. **Recent Advances in Syphilologic Diagnosis and Treatment**

J. H. Stokes. *Pennsylvania Medical Journal* [*Penn. med. J.*] **50**, 718–725, April, 1947. 6 refs.

1950a. **Resistance of Spirochaeta Pallida.** (Om Resistensen af Spirochæta pallida)

I. Baumgarten. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **108**, 1399–1401, Dec. 12, 1946. 8 refs.

Genito-Urinary Disorders

1951. **Abacterial Pyuria with Special Reference to Infection by Spirochaetes**
W. E. Coutts and R. Vargas-Zalazar. *British Medical Journal* [*Brit. med. J.*] **2**, 982–983, Dec. 28, 1946. 23 refs.

The problem of sterile, amicrobic, or abacterial pyuria has been of special interest to these authors, who have published several papers in the Chilean medical journals. They consider that the correct designation for this syndrome should be " abacterial ", and that the syndrome may originate from an ascending or descending infection of the urinary tract by viruses, spirochaetes, or protozoa. Failure to diagnose this condition has been due to the fact that the centrifuged urinary deposit has not been examined by dark-ground illumination as a routine. The authors' first suspicion about the type of organism responsible for the condition was aroused by a case of pyuria in which no organism could be found, but which cleared up on the removal of an infected tooth. The report by Wildbolz to the French Congress of Urology in 1933 of similar cases successfully treated by injection of an arsenical strengthened their suspicion that a search of the urinary deposit by dark-ground illumination might demonstrate spirochaetes.

Five cases are recorded in which urinary symptoms were associated with pyuria but in which no organisms could be found by cultural methods. In each case spirilla were found by dark-ground examination. In every instance the condition was cured by injections of an arsenical. The literature of abacterial pyuria is reviewed. While most of the reported cases have been cured by arsenic, in 1 case only were spirochaetes shown to be the cause of the infection. According to the present authors' observations the bladder and kidneys may become infected by the ascending or descending routes. Spirochaetal (non-syphilitic) infection of the male and female urethra is not uncommon. The descending infection is usually of the blood-stream type. Spirochaetes have been found in bladder urine in so-called war nephritis, trench fever, relapsing fever, and Weil's disease. The authors consider that the spirochaetes present in their cases were derived from the buccal cavity or the intestine. In support of this theory they refer to the literature of spirochaetal involvement of dental structures and to the identification of similar organisms in the alimentary tract. In all their cases the spirilla were of diverse morphology, some being slender with only a few spirals, while others were very similar to *Sp. dentium*. Treatment with quinquivalent arsenicals was always successful. All patients were referred for dental treatment. To demonstrate the presence of these fragile micro-organisms slow and prolonged centrifugation of fresh bladder urine is recommended and the examination of the deposit under dark-ground illumination after the addition of a drop of normal saline at 37° C. which increases the movements of the organisms. *J. E. Semple*

1952. **Treatment of Uremia with Continuous Peritoneal Irrigation**
H. A. Weiss and R. L. Mills. *United States Naval Medical Bulletin* [*Nav. med. Bull., Wash.*] **46**, 1745–1750, Nov., 1946. 10 refs.

Peritoneal irrigation was used in a patient with severe uraemia in an attempt to substitute the excretory activity of the peritoneum for that of the kidneys whose function was failing. Fluid was instilled into one quadrant of the peritoneal cavity at the rate of 25 c.c./min. and removed from the opposite quadrant by means of continuous suction on a sump drain.

The patient's blood urea nitrogen and NPN were reduced a significant amount although the patient subsequently died, largely as a result of a failing myocardium. The fluid removed from the peritoneal cavity contained from 30 to 45 mg. % of urea nitrogen.

No complications arose that could be directly attributed to the peritoneal irrigation. The reduction in blood urea nitrogen and NPN in the case was sufficient that in spite of the fatal outcome we feel the procedure is to be recommended in cases of acute kidney failure where the renal function may reasonably be expected to return to satisfactory levels.—[Authors' summary.]

1953. **Renal Novocain Block in Medical Diseases of the Kidney.** (Il blocco novocainico renale nelle nefropatie mediche. Nota Preventiva)
G. Spadea, G. Fojanini, and P. Frugoni. *Clinica Nuova* [*Clin. nuova*] **3**, 96–110, Aug., 1946. 23 refs.

The infiltration of the perirenal tissue with " novocain " (150 to 200 ml. of a 0·25 to 0·5% solution) blocks the nerve fibres. The temporary results as regards kidney function and increase of diuresis are similar to those obtained by sympathectomy without exposing the patient to the risk of a major surgical operation. Thirteen patients were treated in this manner at the Rome University Clinic, the injection being given unilaterally at the time, but on the contralateral side when repeated. The diagnoses were: acute glomerular nephritis, 7; subacute glomerular nephritis, 1; chronic glomerular nephritis, 2; renal amyloidosis, 1; post-transfusional anuria, 1; anuria in miliary tuberculosis, 1. The patients with acute glomerular nephritis, when seen and treated at an early stage of the disease—that is, within about a fortnight after the onset of the first symptoms—showed increases of diuresis amounting to rises of up to 200% within 24 to 48 hours, and normal diuresis afterwards, whereas in the patients belonging to the other groups the diuresis remained unchanged. The details of the technique will form the subject of a future publication.

[The case reports do not include the figures for the fluid intake.] *L. H. Worth*

1954. **Hypertension of Renal Origin. Case Reports**
G. CARROLL. *Southern Medical Journal* [*Sth. med. J.*] **39**, 761–767, Oct., 1946. 5 figs., 55 refs.

The author reports in detail the case histories of 3 patients with chronic unilateral pyelonephritis and hypertension, in whom removal of the diseased kidney was followed by a return of the blood pressure to normal. The patients remained well after operation throughout follow-up periods of 9 months, 1 year, and 6 years. The author has collected from the literature 86 cases of unilateral nephrectomy in hypertensive patients, and lists only 6 of these as failures. He claims that " the hypertensive juvenile patient with atrophic nephrosclerotic kidney will invariably respond satisfactorily ".

[Although the 3 cases reported seem to be satisfactory examples of " cure " of hypertension by removal of a diseased kidney, the author's review of the literature is unduly optimistic. Of the cases he cites many more than 6 would be generally regarded as failures. Probably the truth lies somewhere between this author's optimistic attitude and the much more cautious view of Goldring and Chasis in their book on hypertension.]

D. A. K. Black

1955. **Lower Nephron Nephrosis. The Renal Lesions of the Crush Syndrome, of Burns, Transfusions, and Other Conditions Affecting the Lower Segments of the Nephrons**
B. LUCKÉ. *Military Surgeon* [*Mil. Surg.*] **99**, 371–396, Nov., 1946. 16 figs., 90 refs.

This investigation was based on 538 fatal cases of kidney failure collected at the U.S. Army Institute of Pathology during the war. The renal lesion was essentially the same in all the cases described, and consisted of a lower-nephron nephrosis. A number of aetiological factors were present. These were divided into eleven groups: battle wounds (221); crushing injuries (46); abdominal operations (36); burns (48); blood transfusion reaction (45); sulphonamide intoxication (47); heat-stroke (19); blackwater fever (14); poisons (20); haemolytic anaemias (4); miscellaneous (38). In many of these groups two therapeutic measures—blood transfusion and sulphonamide administration—were used. Since these agents might induce the lesions, care was taken to separate off such cases. By far the most constant factor was trauma (57%). In the remainder, intravascular haemolysis and severe and prolonged shock were observed.

The clinical manifestations and laboratory findings, whatever the aetiological agent, were essentially similar. Two initial symptoms—shock and vomiting—were constantly seen. The latter was often excessive and might occur at any time during the illness. The main characteristic of the syndrome was oliguria: this was present throughout the entire illness and, in spite of large fluid intake, persisted and sometimes progressed to complete anuria. The urine contained albumin and was highly acid with a fixed specific gravity of 1,014. In the majority of cases a positive benzidine reaction was found even if the urine was not frankly bloody or smoky. The centrifuge deposit contained granular and pigment casts with occasional red blood cells. The chemical composition of the blood suggested " a renal shutdown ". Azotaemia was invariably present, other findings being an increase in serum potassium and phosphate with a lowering of the alkali reserve and blood chlorides. Another cardinal sign of this syndrome was hypertension, which generally appeared about the third day and continued until the end of the illness. The appearance of oedema was variable; it was most often confined to the lower limbs and lungs. The mortality rate was high (90%) and the duration of the illness brief, since three-fourths of the cases died within 8 days. To illustrate the points made in the description of the syndrome 14 cases are quoted.

The author describes in some detail the macroscopical and microscopical findings in the kidney, since little or no changes are found elsewhere in the body. The macroscopical appearance was not, however, pathognomonic, although the weight was increased, especially in cases due to trauma. Slight bulging of the cortex and a contrast in colour between the cortex and medulla were the only changes seen. Four principal features of the histopathological picture are as follows: " (1) Degeneration or actual necrosis, which involves selectively focal portions of the lower segments of the nephrons, i.e., the thick tubules of Henle and the distal convoluted tubules. (2) Edema and cellular reaction which develop in the stroma around the more severely damaged or disintegrated portions of the tubules; these changes are commonly associated with thrombosis of the adjacent veins. (3) Casts of a heme compound which lie within the lumens of variable numbers of the lower segments and of the collecting tubules. (4) Relatively slight or no structural changes in the upper parts of the nephrons—renal corpuscles, proximal and intermediate segments."

The lack of blood in the renal corpuscles was explained by the inadequate blood supply, and the fact that the capsular spaces were not increased was due to a patent nephron. The tubular degeneration varied from frank necrosis to complete disintegration, although the extent of the change was dependent upon the survival period. Usually the lesions were focal and found more commonly in the boundary zone. When the survival period exceeded 3 to 4 days evidence of active cellular regeneration was present. The type of epithelium seen was different from that normally found in these areas and frequently resembled endothelium, later becoming cuboidal. Two types of cast were present, the more conspicuous one being composed of a " heme compound ". These were not considered important. The second type of cast was non-pigmented and hyaline in nature, and was composed of protein. Other microscopical changes found were: (1) oedema and cellular reaction of the stroma, which later gave way to regenerative fibroblastic change, and (2) tubulo-venous ruptures with venous thrombosis. [The microscopical changes described conform essentially to those reported by Bywaters and Dible (*J. Path. Bact.*, 1943, **55**, 7).]

The part played by myohaemoglobin and haemoglobin compounds in causing the renal lesion is discussed under

three headings. First, the method of excretion is dealt with; secondly, the determining factor causing the precipitation of these compounds in the lower segment of the nephron is considered; and, thirdly, the view that such compounds are nephrotoxic is criticized. It is thought that glomerular permeability must be altered to allow the passage of haemoglobin, but it is probable that haemoglobin and myohaemoglobin cause renal vasoconstriction. It is felt that the previous theories with regard to the precipitation of haemoglobin in the presence of acid urine no longer hold, since many authors have shown that fatalities occur equally in the presence of alkaline urine. This problem is still unsolved. The view is held that, provided the solutions are pure, myohaemoglobin and haemoglobin in solution are not nephrotoxic. Haematin, on the other hand, a breakdown product from the various haemoglobin derivatives, may cause the renal lesion by intense vasoconstriction and tubular damage. The same process may be said to follow injury to tissue. In this instance the substance liable to cause such damage is open to question. The part played by physicochemical alterations of the blood is conjectural; there is no doubt that in many conditions which are followed by lower-nephron nephrosis gross disturbances of the metabolites are frequently found. The author feels, however, that disturbances of renal blood flow, in particular renal anoxia, play an important part in the production of this syndrome. In attempting to explain the oliguria, the theory of leakage of glomerular filtrate through the damaged tubular walls was found to fit in best with histological evidence. The idea that extrarenal factors cause this renal lesion was discarded, since in many cases the fault was found to be with the kidney itself.

[This paper is admirably illustrated. It should be read by all those interested in the unsolved problem of acute uraemia.] *E. M. Darmady*

1956. **Observations on Experimental Ammonium Chloride Acidosis**

A. D. T. Govan and J. Parkes. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **58**, 505–515, July, 1946. 9 figs., 12 refs.

Groups of rabbits, 6 in Group A, 6 in Group B, and 2 in Group C were fed on wet bran and oats and were given by stomach tube daily, respectively, 2·5, 3·75, and 5·0 ml. of 20% aqueous ammonium chloride per kg. of body weight. Five rabbits of Group A were killed on the sixth day. The sixth rabbit of Group A, all of Group B, and all of Group C died from necrosis of the renal tubular epithelium after 10 days, 4 to 5 days, and 16 hours respectively. The urine was examined daily for urea, chlorides, phosphates, ammonia, albumin, and *p*H, and the blood for urea, chlorides, phosphates, lipoids, ammonia, carbon dioxide combining power, and *p*H. The lungs, liver, brain, and kidneys were studied histologically. The chemical changes seen in the rabbits in Group A were similar to those observed after therapeutic doses of ammonium chloride. The rabbits that died in Groups A and B had an increased water and urea but decreased phosphate output; the urinary *p*H fell at first but before death rose to the neutral point. The blood urea rose to a relatively low maximum of 120 to 170 mg. per 100 ml. at death. Plasma carbon dioxide-combining power and *p*H fell to 10 to 11 volumes per cent. and to below 7·0, respectively. Plasma ammonia, lipoid, and chloride levels rose to nearly 14 mg., 600 mg., and 700 mg. per 100 ml., respectively. Albumin appeared in the urine whenever the *p*H fell below 6·0, indicating renal dysfunction and suggesting that the results obtained by Bywaters and Stead (*Quart. J. exp. Physiol.*, 1944, **33**, 53) by injecting myohaemoglobin into rabbits previously treated with ammonium chloride could not be entirely attributed to the pigment. Necrosis, which may have been caused by inability to excrete acid, occurred in the distal portion of the nephron and to a lesser extent in the proximal part. The lungs of the rabbits that died were collapsed and contained fat emboli which were probably formed by flocculation of plasma fat at a particular *p*H. *J. E. Page*

1957. **Ethylenediamine Dihydrochloride or "Chlorethamine". I. As a Urinary Acidifier**

E. M. Boyd and J. A. S. Dorrance. *Experimental Medicine and Surgery* [*Exp. Med. Surg.*] **4**, 212–222, Aug., 1946. 14 refs.

This drug (ED) has been marketed in America as a urinary acidifier and diuretic, but no extensive and independent investigations have so far been reported. The authors prefer experiments on animals to experiments on man, since it is difficult to control the diet in man, and this has a definite effect on the *p*H of the urine. The experiments were performed on about 1,000 animals, to many of which the drug was given by stomach tube under light ether anaesthesia. The urine was collected in metabolism cages and its *p*H determined electrometrically. Both ED and ammonium chloride effectively lower the *p*H of the urine—that is, to values around *p*H 6·0—in doses of 0·25 g. per kilo in rats and rabbits; higher doses are required in guinea-pigs. Calcium chloride was highly effective in rats but less effective in rabbits and guinea-pigs. Mandelic acid was very effective in guinea-pigs but not in rats and rabbits. Acid sodium phosphate was of little or no value.

J. M. Robson

1958. **Ethylenediamine Dihydrochloride or "Chlorethamine". II. Untoward and Toxic Reactions**

E. M. Boyd and K. G. W. Seymour. *Experimental Medicine and Surgery* [*Exp. Med. Surg.*] **4**, 223–227, Aug., 1946. 1 ref.

The drugs were given by stomach tube or intramuscularly to more than 2,000 animals, including rats, guinea-pigs, rabbits, cats, and dogs. In rats the LD 50 of "ED" was higher than that of ammonium chloride and calcium chloride and similar to that of mandelic acid and acid sodium phosphate. In oral doses necessary for effective acidification ED caused vomiting in dogs and diarrhoea in all animals; higher doses of mandelic acid also caused diarrhoea. In toxic doses ED produced excitement, irritation, and increased physical activity.

It is concluded that, though the lethal dose of ED is high, undesirable reactions result from doses not much above the therapeutic level. *J. M. Robson*

1959. **Ethylenediamine Dihydrochloride or "Chlorethamine". III. As a Diuretic**
E. M. Boyd and M. S. Lapp. *Experimental Medicine and Surgery* [*Exp. Med. Surg.*] **4**, 228–230, Aug., 1946. 2 refs.

The drugs were given orally (by dropping pipette) to 180 unanaesthetized rabbits in doses of 0·25 g. per kilo in syrup. Some of these animals, as controls, received syrup alone. ED produced a powerful diuretic action lasting for about 5 hours, during which time the urine output was about four times the normal level. Small but more prolonged effects were produced by mandelic acid and calcium chloride. *J. M. Robson*

1960. **Trench Nephritis among Norwegian Civilians.** ("Trench nephritis" blant norsk sivilbefolkning)
A. S. Johannessen and A. Aanonsen. *Tidsskrift for den Norske Lægeforening* [*Tidsskr. norske Lægeforen.*] **66**, 677–679, Nov. 1, 1946. 7 refs.

The authors report 40 cases of acute nephritis which occurred among the Norwegian civilian population in Finnmark (North Norway) during the winter of 1944–5 at a time when large numbers of German troops, just withdrawn from Finland, were billeted on the inhabitants. Of the patients 24 were between 40 and 60 years of age, and 31 were men. In reporting the symptoms the authors emphasize their close correspondence with those normally seen in trench nephritis, and suggest that the civilians were infected by the troops quartered among them. Dyspnoea was seen in 22 cases; bradycardia was seen in 22, hydrothorax and ascites in 29, albuminuria (above ½%) and haematuria in 13, loss of weight greater than 10 kg. in 17, an erythrocyte sedimentation rate above 15 mm. in 22, and eclampsia in 2. Routine treatment, consisting of a low salt and low protein diet, with low water intake (750 ml. daily) and rest in bed, resulted in immediate loss of weight and disappearance of oedema, but the other symptoms persisted for varying periods. As a result of treatment (in 30 cases) 20 became symptom-free, and 3 still had slight albuminuria and 4 gross albuminuria. One patient died in eclampsia, and 2 were subsequently found to have renal tuberculosis.
B. Nordin

1961. **Acute Porphyria**
J. Jørgensen and T. K. With. *Lancet* [*Lancet*] **1**, 54–56, Jan. 11, 1947. 31 refs.

This paper aims at summarizing work on porphyria done in Scandinavia in the last few years. Symptomatic porphyria and congenital porphyria are defined, but not discussed in detail; in both the excreted porphyrin belongs to series I, although small amounts of uroporphyrin III may also be present in the congenital form of the disease, which is also characterized by accumulation of porphyrin in the organs, especially the bones and skin. This paper deals mainly with the third type of porphyria—acute. This disease manifests itself in acute attacks of abdominal pain, vomiting, and constipation, often accompanied by nervous symptoms and dark urine. It is a disease of adults, no case having been reported under 15 years. The urine may not necessarily be dark, as the pigment excretion may be in the form of a colourless precursor of uroporphyrin III, known as porphobilinogen. This is stable in alkaline urine, but changes in acid urine to a mixture of porphobilin and uroporphyrin III, giving a dark colour to the urine. Porphobilinogen gives the same reaction with Ehrlich's reagent as does urobilinogen, but is not extracted by ether from acidified urine. This pigment may occur in the urine of people who have no clinical symptoms (latent porphyria); in some cases of this type the excretion of abnormal pigment is intermittent. Barbiturates may provoke attacks in patients with latent porphyria. The authors describe 2 patients, 1 with latent porphyria in whom phenobarbitone provoked an attack, and 1 with manifest porphyria who died a few days after an injection of 0·35 g. soluble barbitone. In the first patient, a provocative course of phenobarbitone given after recovery from the acute attack was followed by reappearance of porphobilinogen in the urine. The paper describes a method of assaying porphobilinogen in terms of extinction units in the Pulfrich photometer.

[This paper is a useful summary of Scandinavian work on acute porphyria. Some of the conclusions are debatable, as, for instance, that the pigments excreted in this condition are mainly of series III, and that there is no accumulation of porphyrins in the tissues.]
D. A. K. Black

1962. **A Note on Genital Fusospirochetosis**
M. Lev and E. B. Tucker. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **16**, 401–404, June, 1946. 4 figs., 6 refs.

Fourteen cases of fusospirochaetal disease were seen in a series of 800 patients presenting themselves with penile lesions for dark-ground examination. The lesions were generally multiple, tender, superficial erosions or ulcerations with soft edges and red granular bases, situated in the coronary sulcus and the adjacent parts of the prepuce and corona. The diagnosis rested on the demonstration on dark-ground examination of borrelia-like spirochaetes with characteristic motility, and gentian-violet-stained smears of the lesion showing the characteristic spirochaetes, accompanied by fusiform bacilli, vibrios, cocci, and a relatively small number of neutrophils. In most instances the infection appeared to be primary. Brief reference is made to the literature on this subject. *A. Henderson-Begg*

1963. **Functioning of the Fetal Kidney as Reflected by Stillborn Infants with Hydroureter and Hydronephrosis**
L. J. Wells and E. T. Bell. *Archives of Pathology* [*Arch. Path.*] **42**, 274–276, Oct., 1946. 25 refs.

1963a. **The Management of Urinary Infections**
D. Swartz. *Manitoba Medical Review* [*Manitoba med. Rev.*] **27**, 205–212, April, 1947. 17 refs.

Locomotor Disorders

1964. **A Further Report of an Epidemic of Acute Polyarthritis**
G. GOSWELL. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 861–863, Dec. 21, 1946. 5 refs.

An epidemic is reported, in a Royal Australian Air Force unit stationed in Australia, of a mild acute polyarthritis associated with lymphadenitis and a transient exanthem. Three similar outbreaks had occurred previously in the same area. The report is based on 51 cases, and gives a detailed account of the clinical features. Illness was mild with little or no malaise, and with pyrexia only in the more severe cases; 16 required in-patient treatment. The duration ranged from a few days to several weeks; more than half had completely recovered by the seventh day. A dull aching and a feeling of stiffness in several joints were the initial symptoms. Pain had abated within 4 or 5 days; residual stiffness quickly responded to exercise, leaving no joint sequelae. In the first few days joints were tender, but in only 15 cases was there any swelling from synovial or periarticular effusion. Tender enlarged lymph nodes, especially in the axillae and inguinal regions, were usual. A generalized papular rash was observed in 3 cases, beginning 24 to 48 hours after the onset and disappearing by the fourth day. Twelve patients had pyrexia for 4 to 6 days, temperatures usually ranging from 99·6° to 100·6° F. (37·5° to 38·1° C.). On clinical grounds it was thought possible to exclude a dysenteric arthritis, the joint manifestations of dengue, acute rheumatism, and rheumatoid arthritis. Laboratory investigation of the epidemic was not practicable. *Kenneth Stone*

1965. **Still's Disease Successfully Treated with Prostigmine. Report of Case**
M. RITTWAGEN. *Archives of Pediatrics* [*Arch. Pediat.*] **63**, 630–638, Dec., 1946. 27 refs.

An 11-year-old coloured girl was suffering from a severe degree of Still's disease. She had been treated without success with salicylates given both by mouth and intravenously, with large doses of sulphonamides, with intramuscular and intravenous penicillin, and with massive vitamin-D therapy. These treatments had been given in addition to general measures, repeated blood transfusions, and physiotherapy. When all these had failed and the pain persisted it was decided to treat the patient with oral and intramuscular prostigmin with a view to relieving the pain due to muscle spasm. She was given intramuscular injections of prostigmin methyl sulphate [the dose is given as " one ampoule, 1–2,000, three times daily "] and 15 mg. of prostigmin bromide by mouth once daily for 2 months. The intramuscular doses were then stopped, and the oral doses increased and later decreased. At the same time orthopaedic measures were taken which consisted of tenotomies and plaster splinting. The response to treatment with prostigmin was almost immediate, and after 5 months all signs of activity of the disease had disappeared and function was very good. The author discusses the manifestations and differential diagnosis of Still's disease. The patient described had had an attack of pericarditis which cleared up uneventfully. No new light was thrown on the aetiology of the condition.

W. Tegner

1966. **Rheumatoid Arthritis. I. Introduction to a Study of its Pathogenesis**
A. D. WALLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 713–715, Dec., 1946. 16 refs.

1967. **Rheumatoid Arthritis. II. Non-specific Serologic Reactions**
A. D. WALLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 716–717, Dec., 1946. 6 refs.

1968. **Rheumatoid Arthritis. III. The Pneumococcus Antibodies**
A. D. WALLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 718–722, Dec., 1946. 15 refs.

The current medical view that true rheumatoid arthritis is due to infection is open to criticism. It is based chiefly upon superficial resemblances between rheumatoid arthritis and certain infectious arthritic processes such as gonococcal arthritis. Rheumatoid arthritis has now emerged as a clinical entity distinct from other types of polyarthritis in which the causation may reasonably be inferred to be metastatic from a focus of infection, but aetiological confusion still persists. Moreover, certain serological observations have been interpreted as supporting an infective aetiology in rheumatoid arthritis. The author, who is Research Fellow in Arthritis in the University of Pennsylvania, has examined the foundations of the bacterial theory, and more specifically the haemolytic streptococcal theory, of the origin of rheumatoid arthritis, and has found them to be insecure. In his selection of material for this investigation he used only typical cases of at least a year's duration and with symmetrical involvement of the proximal interphalangeal joints of the fingers.

The general arguments against a bacterial origin which he quotes are as follows: The presence of bacteria of any species has not been consistently demonstrable in the blood of patients with rheumatoid arthritis. The extraordinary prolongation of the active stage of the joint lesions in this disease and their tendency to symmetry are arguments against bacterial aetiology in general, and their indifference to both sulphonamides and penicillin is against a streptococcal aetiology in particular. With regards to antistreptolysin and antifibrinolysin tests, these antibodies were not found in significant titre, and were never comparable with those found in cases of acute

rheumatic fever or in known haemolytic streptococcal infections. The sera of many patients with well-established rheumatoid arthritis, moreover, have a tendency to precipitate in the saline control tube of a precipitin test, especially after centrifugalization. He points out that many rheumatoid arthritis sera also differ from the normal in being able to agglutinate suspensions of fine collodion particles. From these observations he concludes that supposedly specific reactions in which the serum of patients with rheumatoid arthritis takes part should be interpreted with considerable caution.

Having regard to these facts, and apparently dependent on them, the author found that the sera of patients with rheumatoid arthritis will precipitate the somatic carbohydrate of the pneumococcus a little more strongly than does the serum of non-arthritics. In the same way the rheumatoid serum also agglutinates non-encapsulated pneumococci a little more strongly. He explains these findings as being due to a non-specific enhancement of the action of normally present antibodies to Gram-positive cocci of many types. He considers: (1) that the making of a distinction between true rheumatoid arthritis and arthritis of other types, particularly that which is secondary to a focus of infection, is of great importance; (2) that the foundations of the bacterial theory, and more specifically the haemolytic streptococcal theory, of causation of true rheumatoid arthritis are insecure; (3) that supposedly specific reactions in which serum from patients with rheumatoid arthritis is employed should be suspect; and (4) that the increased ability of such serum to agglutinate other Gram-positive cocci, such as the pneumococcus, appears to be due to a non-specific increase in the action of normally present antibodies. *W. S. C. Copeman*

1969. **A Therapeutic Score Card for Rheumatoid Arthritis. A Standardized Method of Appraising Results of Treatment**
O. STEINBROCKER and A. BLAZER. *New England Journal of Medicine* [*New Engl. J. Med.*] **235**, 501–506, Oct. 3, 1946. 3 refs.

The authors have devised a " therapeutic score sheet " as a means of assessing the results of treatment in chronic rheumatoid arthritis. Their method is to take a number of the chief features of rheumatoid arthritis and to allot debit marks to each feature. If any feature is absent no debit marks are recorded. The total debit marks subtracted from 100 represents the patient's index number as a percentage of normal; a rise in this figure gives a measure of the patient's improvement. At the first examination each feature, even if present in slight degree, is awarded the maximum debit marks, and these are reduced at subsequent examinations if improvement has occurred. Thus, apart from the appearance of a new feature, there is no provision for recording a deterioration. The features selected are active joint swelling, sedimentation rate, articular mobility, joint tenderness, weight gain (or loss), haemoglobin, pain, well-being, and functional capacity.

Active joint swelling is regarded as the crucial sign of rheumatoid arthritis and is debited 50 marks at the original examination. At subsequent examinations the debit may be reduced as far as 40, but never below this while any trace of active swelling remains. Active swelling must be carefully distinguished from any permanent thickening of the joint. Rates of 15 mm. by the Cutler method and 25 mm. by the Westergren are taken as bases for the sedimentation rate. A rate at or above these levels requires the maximum debit of 15 marks. The debit is not increased if the rate should rise, but a proportionate reduction is made if it should fall. All the other features carry a maximum debit of 5 marks each, giving a possible total of 100 debit marks. The standard haemoglobin level is taken as 80%. Four case histories with their appropriate score sheets are given, showing 1 case of complete recovery with a final score of 100 and the remainder with varying degrees of improvement. The authors claim that their scheme provides a universally understandable and comparable set of criteria which, even if derived from different observers, gives reliable information for the evaluation of therapeutic agents. *H. F. Turney*

1970. **The Heart in Rheumatoid Arthritis**
A. S. ROGEN. *British Medical Journal* [*Brit. med. J.*] **1**, 87–88, Jan. 18, 1947. 12 refs.

The author reviews recent work on the aetiological relationships between rheumatic fever and rheumatoid arthritis, with special reference to the cardiovascular system. The main part of the paper is concerned with an examination of the cardiovascular system in 33 consecutive cases of rheumatoid arthritis; 22 of the patients were females. Careful search was made for evidence of mitral stenosis but none was found. In 1 case only, a woman of 68, was there a loud apical systolic bruit which was considered to be organic; in 8 cases there was a functional murmur. The electrocardiograms of 29 patients showed no changes that could be held to be suggestive of rheumatic fever, though in some cases there were T-wave changes corresponding in all probability to the state of arterial degeneration occurring in old people, who formed the majority of the patients in this series. No macroscopical or histological changes of rheumatic fever were seen in the 1 case which came to necropsy.

These results are at variance with the reports of some, but not all, workers, and serve to emphasize the limited value of comparisons between the clinical manifestations of rheumatic fever and rheumatoid arthritis in the present state of our knowledge of the rheumatic diseases. *James W. Brown*

1971. **A Rare Cause of Dysphagia: Cervical Spondylitis.** (Une cause rare de dysphagie: La spondylose cervicale)
R. POINSO and J. CHARPIN. *Revue du Rhumatisme et des Maladies Ostéo-articulaires* [*Rev. Rhum.*] **13**, 327–330, Nov., 1946. 2 figs., 8 refs.

A male aged 47 had suffered for 18 months from an ankylosing polyarthritis, probably of tuberculous origin, with involvement of most joints and also of the spine. During this period he had noticed difficulty in swallowing

solid food and had located the obstruction at the root of the neck.

The radiological examination of the spine showed decalcification of the vertebral bodies, with numerous osteophytes bridging the intervertebral spaces, especially between the second and third and the fifth and sixth cervical vertebrae. At the latter level a rather large, partially calcified projection 6 to 7 cm. in height spread out in front of the spine. There was no continuous calcification of the anterior vertebral ligament. Other possible causes of dysphagia were excluded, and after discussing the part played by spasm the authors conclude that in their patient the dysphagia was due to direct compression of the pharynx by the vertebral osteophytes.

T. G. Reah

1972. **Fibrous Dysplasia of Single Bones (Monostotic Fibrous Dysplasia)**

H. G. SCHLUMBERGER. *Military Surgeon* [*Mil. Surg.*] **99**, 504–527, Nov., 1946. 34 figs., 26 refs.

Sixty-seven cases of fibrous dysplasia involving a single bone are reported. This disease is a separate entity from other forms of fibrous dysplasia of bone (osteitis fibrosa), is not a congenital anomaly, and aetiologically has nothing in common with Albright's syndrome, which is a polyostotic fibrous dysplasia associated with pigmentation of the skin, and precocious puberty in females. There was neither pigmentation nor endocrine disturbance in the cases reported in this article, and only 5 of the patients were women. The latter fact, however, is of no statistical significance, because the cases were collected among U.S. Army personnel or among recruits.

The first sign of monostotic fibrous dysplasia was usually a local swelling of bone associated occasionally with tenderness or arthritic pain referred to the nearest joint. In a few cases the condition was discovered only after a pathological fracture had occurred. Serum calcium, phosphorus, and phosphatase determinations were made and found to be normal in 18 of the patients. The prognosis is good; simple excision if the lesion is in a rib, or curetting followed by filling of the defect with bone chips if it is in a long bone, yields satisfactory results. There is no evidence that the monostotic form of fibrous dysplasia may progress to the polyostotic form. The radiological findings are entirely non-specific. In skiagrams the area of fibrous dysplasia is radio-translucent and sometimes traversed by delicate bony trabeculae. It is usually central in position and produces thinning and expansion of the cortex.

The pathological features of the condition were studied in 18 resected ribs. The lesions appeared as a fusiform or spherical swelling up to 6 cm. in diameter. The surface consisted of thinned-out but otherwise intact cortical bone. The cancellous bone and bone marrow of the rib were replaced by a firm yellow-white tissue occasionally containing small cysts. Histologically this yellow-white tissue was seen to be a fairly well vascularized connective tissue arranged in interlacing bundles and whorls. Within this tissue there was frequently metaplastic bone formation. Islets of cartilage were not observed except in conjunction with healing pathological fractures. The frequency of the involvement of the various bones was as follows: ribs 29, femur 9, tibia 8, maxilla 7, calvarium 5, mandible 2, humerus 2, ulna 2, vertebrae 1, pelvis 1, and fibula 1. For each group of bones representative case histories are given. It is suggested that the so-called ossifying fibroma and non-osteogenic fibroma of bone are variants of fibrous dysplasia and that monostotic fibrous dysplasia may represent a disturbance of the normal reparative processes of bone after injuries. The lesions are well illustrated by skiagrams and photomicrographs, some of which are in colour.

G. Popják

1973. **Osteomalacia and Late Rickets. The Various Etiologies Met in the United States with Emphasis on That Resulting from a Specific Form of Renal Acidosis, the Therapeutic Indications for Each Etiological Sub-group, and the Relationship Between Osteomalacia and Milkman's Syndrome**

F. ALBRIGHT, C. H. BURNETT, W. PARSON, E. C. REIFENSTEIN, and A. ROOS. *Medicine* [*Medicine, Baltimore*] **25**, 399–479, Dec., 1946. 39 figs., 56 refs.

The authors define osteomalacia as a disorder of bony tissue in which there is failure to deposit calcium salts in newly formed osteoid tissue, because of an imbalance between the levels of calcium and of inorganic phosphorus in the body fluids. Chemical examination of blood serum shows a normal or a low level of calcium, a low phosphorus level, and a high alkaline phosphatase level.

Milkman's syndrome in which there are multiple spontaneous idiopathic symmetrical fractures is considered to be one form of osteomalacia, and evidence, including some histological studies, is given for this belief. Six fresh cases of this syndrome are described, and attention is drawn to the frequency of united but uncalcified fractures of the scapulae just below the glenoid cavities. Results of treatment are given.

A discussion on the mode of action of vitamin D leads to the conclusion that it has two main effects: it increases the absorption of calcium from the gut and increases the excretion of phosphate by the kidney. These two activities are shown in varying degree in different individuals and with different doses. Dihydrotachysterol has the same two pharmacological actions as vitamin D but the effect on phosphate excretion is relatively greater. The authors therefore suggest that dihydrotachysterol is the agent of choice in the treatment of hypoparathyroidism, and vitamin D the choice in the treatment of osteomalacia.

A long discussion of renal acidosis resulting from tubular insufficiency without glomerular change is illustrated by the findings in 6 fresh cases. The resulting osteomalacia responded remarkably well to treatment with vitamin D and an alkalinizing salt such as sodium citrate; in order to prevent recurrence it was necessary to continue the use of the citrate after return of the bone to normal. Many other points of interest to biochemists and physicians are discussed in this very long paper.

H. E. Harding

Neurology and Psychiatry

1974. **On Delirium Acutum with Special Reference to Biochemical Changes.** [In English]
K. HERMANN and O. LUND. *Acta Psychiatrica et Neurologica* [*Acta psychiat. Kbh.*] **21**, 329–348, 1946. 3 figs., 30 refs.

The authors describe 5 cases of acute delirium of uncertain causation. Biochemical investigation suggested that neither acidosis nor raised blood lactic acid nor acetonuria could be held responsible for the psychiatric picture, though blood urea is raised in the more exhausted patients. The pyruvic acid content of the blood is considerably raised in proportion to the severity of the clinical picture, which coincides with a fall in blood citric acid. These findings are interpreted as being due to disturbances of carbohydrate metabolism in no way specific for acute delirium, though perhaps an essential accompaniment to the disorder.

[The English in this article is by no means always easy to understand.] *Hugh Garland*

1975. **Neuroectodermal Tumours Containing Neoplastic Neuronal Elements: Ganglioneuroma, Spongioneuroblastoma and Glioneuroma. With a Clinicopathologic Report of Eleven Cases, and a Discussion of Their Origin and Classification**
H. KUHLENBECK and W. HAYMAKER. *Military Surgeon* [*Mil. Surg.*] **99**, 273–292. Oct., 1946. 56 figs., 42 refs.

Two cases of ganglioneuroma of the thoracic cavity, 1 of glioma of the eye, and 8 gliomata of the brain are described. Some excellent photomicrographs are reproduced. The authors designate the 8 cerebral tumours as "spongioneuroblastomas" and "glioneuromas" because they believe neuroblasts or differentiated nerve cells to be present in them.

[In the abstracter's opinion, however, with the possible exception of the peculiar tumour in Case 4, these brain tumours were gliomata of the ordinary kinds, in which large tumour astrocytes or included nerve cells have been mistaken for tumour nerve cells. The writers have insufficiently appreciated the diversity of appearances which neoplastic astrocytes can assume.]

R. A. Willis

1976. **Ataxia of the Legs and Loss of Vibration: An Isolated Spinal Syndrome**
L. HALPERN. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **104**, 474–479, Nov., 1946. 1 ref.

The author describes 6 cases which presented identical symptoms of ataxia in the legs and absence of vibration sense in the areas supplied by sacral and lumbar segments. There were no other objective neurological findings of a motor or sensory nature, although slight paraesthesiae occurred in the legs at the onset in 4 cases. Position sense was intact in all and there were no changes in reflexes. In 3 cases a mild infection preceded the onset of ataxia—diarrhoea in 2 and tonsillitis in 1. The only positive laboratory finding was a slight increase in the protein content of the cerebrospinal fluid, 2 cases only showing positive Pandy and Nonne-Apelt reactions. The cell content of the fluids was normal in all cases. The ataxia had usually disappeared by the end of 6 weeks, and the vibration sense usually returned during the third week.

The author regards these cases as having an affection, hitherto not described, of the tract of Goll, involving only certain elements. He excludes vitamin deficiency and peripheral neuritis as causes, and prefers not to regard the cases as examples of "acute infective polyneuritis", Guillain-Barré syndrome, although the presence of albumino-cytological dissociation in the cerebrospinal fluid suggests that they might be examples of this condition. *J. MacD. Holmes*

1977. **On the Treatment of Tabes Dorsalis with Artificial Fever (Hyperthermia Treatment).** [In English]
J. BOAS. *Acta Psychiatrica et Neurologica* [*Acta psychiat. Kbh.*] **21**, 39–55, 1946.

Eleven cases of tabes dorsalis have been treated by artificial pyrexia, given usually in the out-patient department in 10 sessions of 3 hours each; 8 patients were complaining of lightning pains and 3 of gastric crises. All had been previously treated with antisyphilitic drugs. Of the 8 with lightning pains only 1 failed to show any improvement, though treatment had to be repeated in some. All 3 cases with gastric crises showed improvement over a short period of observation. Treatment was not followed by exacerbation of pain.

[Although the series is small the results are quite impressive.] *Hugh Garland*

1978. **On the Psychopathology of Disseminated Sclerosis.** [In English]
N. C. BORBERG and V. ZAHLE. *Acta Psychiatrica et Neurologica* [*Acta psychiat. Kbh.*] **21**, 75–89, 1946. 5 refs.

A psychiatric study has been made of 330 recent cases of disseminated sclerosis; of these 47·3% had developed mental symptoms. Neurological findings were qualitatively the same in those with mental symptoms and those without; the more severe motor and sphincter disturbances occurred in the psychopathological group, the respective figures for severe motor symptoms and sphincter disturbances being 39·5% against 21·4%, and 60·5% against 42·8%. Of the total, euphoria was found in 33% and in 69·2% of those with psychiatric change; dementia occurred in 14% and 29·5% respectively, euphoria and dementia together in 8·5% and 17·9%. The figures demonstrate a parallel between the degree of

euphoria and the severity of paralysis, sphincter disturbance, and spinal-fluid change. Mental symptoms developed in 41·6% of cases within the first 3 years.

[The references are entirely to Continental literature, and there is no reference to the important paper of Cottrell and Kinnier Wilson written in 1926. The experienced neurologist will find nothing surprising or new. There is a good deal of psychiatric jargon, and many will not be familiar with such terms as " isophene ", " erethism ", and " ixothymiac "; nor is such a word as " diagnostication " to be encouraged.] *Hugh Garland*

1979. **Spina Bifida and the Cerebrospinal Fluid**
G. B. HASSIN and T. HARRIS. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **5**, 309–320, Oct., 1946. 8 figs., 23 refs.

In collaboration with his co-worker, Hassin, who holds the unorthodox view that the choroid plexus has nothing to do with the manufacture of cerebrospinal fluid, Harris discusses the causes of the cystic tumour-like protrusion in spina bifida. On the basis of a study of 6 cases the conclusion is reached that the herniated sac so often found in this condition is a distended subarachnoid space caused by excessive accumulation of spinal fluid; the excess is considered to be due, not to over-production, but to defective absorption. The perineural spaces of the spinal roots within the sac and those of the spinal ganglia and of the postganglionic peripheral nerves provide avenues for the escape of cerebrospinal fluid. Their gradual obliteration at levels where there are neither dura nor vertebrae to support the spinal cord and arachnoid is the cause of the protrusion. The process is essentially a destructive one and is not a manifestation of an embryonic defect, as was formerly assumed. The mechanism of internal hydrocephalus in spinal bifida is merely an accidental and distant complication brought about by the so-called Arnold-Chiari malformation, itself probably secondary to traction on the medulla oblongata or cerebellum or both. *R. M. Stewart*

1980. **The Syndrome of the Auriculotemporal Nerve**
L. J. KARNOSH. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **13**, 194–198, Oct., 1946. 1 fig., 5 refs.

This syndrome was first described in 1923 by Frey in a patient who had suppurative parotitis after typhus. The condition follows some months or even several years after a parotid abscess. The patient notes that when he begins to eat, especially if the food is hot, spicy, dry, or sour, there is deep boring pain in front of the tragus and over the lower jaw and same side of the tongue and throat, accompanied by redness of the skin and profuse perspiration over the region of the parotid gland, while the mucous membrane of the mouth on the same side is abnormally dry. Similar symptoms can be caused by stimulation of the posterior third of the tongue on the same side with a sour substance. On examination there is blunting of tactile sensation in the distribution of the auriculo-temporal nerve. Although an ipsilateral facial palsy is frequently present as a result of damage to the nerve in the substance of the parotid gland, this is not an integral part of the syndrome.

The auriculo-temporal nerve contains somatic afferent fibres, vasodilator fibres, and secretory fibres for the parotid gland and for the sweat glands; the parotid fibres are para-sympathetic and reach the auriculo-temporal nerve from the glossopharyngeal by way of the otic ganglion. The sudomotor fibres are derived from the cervical sympathetic. The explanation of the syndrome which the author accepts is that the capsule of the parotid gland is damaged by the suppurative process and the fibres of the auriculo-temporal nerve are disorganized. When regeneration of the nerve takes place some of the parotid para-sympathetic fibres become connected with end-organs in the skin, sweat glands, and arterioles instead of taking their normal course to the parotid gland. As a result, when the patient eats, a volley of nerve impulses reaches these end-organs and causes sweating and vasodilation instead of normal salivation. A similar syndrome may at times occur after excision of a mixed parotid tumour for a similar reason. Two typical cases are described occurring 2 years and 11 months respectively after metastatic suppurative parotitis. Atropine relieved the symptoms in the first case.

J. W. Aldren Turner

1981. **The Application of Electromyography to Affections of the Facial and the Intrinsic Laryngeal Muscles**
B. FEINSTEIN. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **39**, 817–819, Oct., 1946. 7 refs.

Electromyography was applied to 150 cases of facial paralysis. It was found possible to distinguish between cases due to temporary ischaemic block—in which complete recovery can be expected—and those due to interruption of the axons. In these latter cases recovery was slower and associated movements occurred. This differentiation between ischaemic block and axonal interruption cannot be made until 12 to 14 days after the onset of paralysis as it is not until then that fibrillation commences in cases of axonal interruption. Facial paralysis following a head injury is, in the majority of cases apparently, due to an ischaemic block. Even in cases where axonal interruption is demonstrated by electromyography, provided there is no gross displacement of the nerve, such as might be demonstrated radiologically in cases of fracture and displacement of the mastoid process, 6 months should elapse before exploration and grafting of the nerve are considered, since re-innervation usually occurs.

In facial paralysis of the infective group (Bell's palsy, herpes, and otitis media) electromyographical examinations confirmed the clinical observations. In both the traumatic and infective groups electromyography was particularly valuable in assessing the prognosis by detecting minimal degrees of re-innervation before the return of functional recovery. Two cases of the infective group with complete axonal interruption were treated with daily galvanism and massage; soon after the weekly electromyograph had demonstrated the first motor unit action potentials, galvanism was stopped and was

replaced by active movements in front of a mirror. It is thought that by this means the associated movements present on recovery were diminished.

In the larynx electromyography was used to differentiate between paralysis of the intrinsic muscles and immobility of the vocal cords due to fixation of the crico-arytenoid joint. For this purpose a concentric needle electrode of sufficient length to be used through a laryngoscope was employed. *Norman W. MacKeith*

1982. **Pathogenesis of Guillain-Barré's Syndrome.** (Beitrag zur Pathogenese des Guillain-Barré'schen Syndroms)
G. SMIROS. *Klinische Medizin* [*Klin. Med., Wien*] **1**, 455–459, Sept. 1, 1946. 8 refs.

The polyneuritic syndrome described in 1916 by Guillain, Barré, and Strohl is characterized by flaccid paralysis of the limb muscles with loss of tendon reflexes, paraesthesiae, slight sensory disturbance, and changes in the cerebrospinal fluid consisting of a considerable increase in the protein content, caused by plasma which passes from inflamed capillary vessels into the spinal fluid. The syndrome has been called polyradiculoneuritis, inflammatory polyneuritis, and polyradiculitis. Bannwarth considers the syndrome to be a consequence of serous inflammation in the cerebral and spinal fluid. The author agrees with Bannwarth, who thinks serous and allergic inflammation identical, that any toxin producing a serous or allergic inflammation can also cause inflammatory polyneuritis with the Guillain-Barré syndrome. Very often it results from a throat infection. The changes in cerebrospinal fluid prove that the polyneuritis is not confined to the peripheral nerves, but that the nerve roots are especially affected.

The author reports a case of inflammatory polyneuritis with the Guillain-Barré syndrome. A 36-year-old woman 8 days after a throat affection developed paraesthesiae in the hands, with weakness and pains in the legs. The next day she had paralysis of the four limbs with increased pain. The patient complained also of dimness of vision. Clinical investigation showed a well-nourished woman, with flaccid paralysis of all four limbs, loss of reflexes, and atrophy more distal than proximal. There was tenderness on pressure of the brachial plexuses and the big nerve trunks of the limbs. Tactile sensibility was slightly lowered. She had a stiff neck, with Kernig's sign positive. Her temperature was 37·2° C. Examination of the cerebrospinal fluid gave a positive Pandy (+++) reaction and positive Nonne-Apelt (++) reaction with no increase in cells; the Wassermann test in fluid and serum was negative. Blood examination was normal. The case was especially interesting, in that the fundus oculi showed abundant superficial haemorrhages, originating from an oedematous infiltration of the papilla, with congestion in the papillary vessels. During the first month of her stay in hospital there was mild rise in temperature and increase of the atrophy, especially of the hands, with a complete reaction of degeneration. However, within 3 months after "vaczineurin" injections, large doses of vitamin B, and electrical treatment, there was decisive improvement; she had no pain and the paralysis was nearly gone, although the hands were still atrophic and paretic. After another 3 months the patient was able to walk, and the last examination of the cerebrospinal fluid was normal. The examination of the fundus oculi showed hardly any residual changes; all the haemorrhages had disappeared. The changes in the fundus oculi in this case justify the conclusion that oedematous infiltration and haemorrhages into the peripheral nerves, produced by disturbances of the blood vessels, had caused the neuritis, and that the Guillain-Barré syndrome resulted from a serous inflammation. *Paul Mayer*

1983. **The Problem of Disseminated Sclerosis**
D. MCALPINE. *British Medical Journal* [*Brit. med. J.*] **2**, 587–588, Oct. 19, 1946.

In his presidential address to the Section of Neurology of the Royal Society of Medicine, McAlpine considered the problem of the aetiology of disseminated sclerosis. Inheritance plays only a minor role, the choice lying between a biochemical or enzymic abnormality (of which proof is lacking), or a toxic-infective process. Clinical and histological studies of the disease and of various forms of virus encephalitis in man and animals suggest an infective agent. The relapsing nature of the disease might suggest an allergic basis. Bacteriologists have failed to find a causal agent, which fact seems to point to a filter-passing virus rather than to bacterial invasion. This is perhaps supported by recent work in Moscow, not yet published in Britain, which claims isolation of a virus from a human case and production of the disease in animals. Invasion may take place months or years before the first sign of the disease. The skin or the alimentary tract are the likeliest portals of entry, and a neural or haematogenous spread from the focus is a necessary postulate. "The fact that a history of intestinal disorder is rarely found in these cases must not be regarded as a reason for dismissing this possibility".

Supported by 124 of his own cases, seen in the last year, McAlpine considers causation from the clinical approach. Only in Britain is the disease held to be commoner in females; the series supports this, particularly in the fifth decade of life. Occupation plays no part, nor is there a seasonal incidence. Familial cases occurred in 8, or 5%, of 142 of his cases (including the 124 referred to above); in 6 the disease affected siblings, and in 1 case the father and in another the mother of the patient. Occasional hereditary predisposition makes the position comparable to that of tuberculosis. Neither body build nor colouring are significant though obesity appears to give some protection. Approximately 20% of the patients had "felt run down" before the illness began; in only 8 was there a history of any fever—usually described as "influenza"—within a month of onset, and in only 5 others a history of a "cold and sore throat" without fever. A positive history of peripheral sepsis within 1 year of the onset was obtained in 18 cases. The possibility of secondary virus infection was not excluded. McAlpine concluded: "There is urgent need for carefully planned research work based on the close co-operation of the clinician and bacteriologist". *Denis Hill*

1984. **Analysis of One Hundred Cases of Epilepsy**
O. MARBURG and M. HELFAND. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **104**, 465–473, Nov., 1946.

This is a report of the study of 100 selected cases of epilepsy over a long period. Factors of aetiological significance were discovered in only 28 cases, and head injury was thought to be the most important factor in 20 cases. The relative value of phenobarbitone, phenytoin (" epanutin "), and methylphenylethyl hydantoinate (" mesantoin ") in treatment is discussed.

[This paper contributes nothing new to our knowledge of epilepsy or its treatment.] *J. MacD. Holmes*

See also *Abstr. World Surgery*, 1947, **1**, 316.

PSYCHIATRY

1985. **On the Nature of Fear**
D. O. HEBB. *Psychological Review* [*Psychol. Rev.*] **53**, 259–276, Sept., 1946. 42 refs.

During experiments on the individual behaviour of chimpanzees interesting observations having wide significance were made on fear reactions. These reactions were withdrawal immediately following perception of the test object, keeping a distance when the test object was moved, and accompanying screaming and erection of hair. Several varied test objects were used, but those significant for this study were parts of chimpanzees, such as an isolated head, or an immobile (anaesthetized) or dead chimpanzee. These produced marked fear reactions. Arguments are adduced to show that the fear of such objects is spontaneous, and that it is not due to previous learning or conditioning. Similar objects commonly produce spontaneous fear in human beings, and many situations seem to evoke spontaneous fear as opposed to fears founded on experience or conditioning. Such spontaneous fears do not seem to depend only on sensory presentation, for a detached head evokes quite a different reaction from a head with the body hidden. We cannot assume that, since a whole body does not excite fear while a detached head does, the rest of the body normally inhibits the fear response. It would seem, then, that the fear is induced by the interaction of sensory events with other cerebral processes. This is exemplified by a study of fears induced by noise or lack of support. It is the suddenness of the noise or of being dropped that evokes fear—that is, a relationship of the excitation to concurrent cerebral activity. This is borne out by a study of the electrical activity of the brain, which is continuous. An affective excitation does not arouse inactive tissue, but modifies an activity already in existence. It is suggested that fear occurs when an object is seen which is like familiar objects in enough respects to arouse habitual processes of perception, but in other respects arouses incompatible processes. This involves a " conflict " hypothesis, but this will not explain all fears, such as fear of darkness when a negative perception is operative. Disorganization of cerebral activity, which might be caused by " conflict " or absence of a customary sensory stimulus, might be a better explanation of fear, since this could explain the various manifestations of fear reaction and the modification of these by learning. Fear may be elicited by a disruption of a co-ordination principally acquired in the timing of cellular activities in the cerebrum. Fears may be due to conflict, the sensory defect, or to constitutional disturbances, such as the fears in pellagra due to organic cellular changes which may or may not be reversible. Such changes due to endocrine factors may explain the emotional instabilities of youth. Fear is related to rage, and rage may be a different form of disorganization of cerebral activity. This hypothesis may be extended to explain all sorts of emotional reactions, and why in psychoses similar responses may be produced either by severe and prolonged conflict or by metabolic changes. *R. G. Gordon*

1986. **Psychology and Treatment of Alcoholism**
H. M. TIEBOUT. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **7**, 214–227, Sept., 1946. 3 figs., 1 ref.

The author thinks that man's essential nature or self " is that whole area of feeling and of impulse . . . which has the problem of somehow living and functioning in the world ". In the normal person, a floating or diffuse boundary is set up between the self and the environment, " to create some privacy for his inner life, for motivations, reflections, and emotions ". This boundary only interferes slightly with in-coming stimuli and out-going impulses. It has qualities of rigidity or flexibility, permeability or impermeability, and capacity to shift from one quality to another as inner or outer circumstances may require.

In incipient alcoholism the boundary is drawn more tightly, and the free relationship between the individual and reality is reduced so that he tends to live more within himself. As the alcoholism develops, more and more gaps are closed until a barrier seems to be erected, a hard shell round the inner self. Then, out-going impulses are blocked, causing unrelieved tension: incoming stimuli are blocked causing lessened awareness of reality; and the fully developed alcoholic is egocentric, living within a barrier which separates him from the world.

The author's formulations are based on experience of about 250 alcoholic in-patients, many of whom were afterwards treated as out-patients. Before a spree patients complain of tension; during the spree there is a feeling of release and sensation, thought and action flow freely—the barrier has been thrown out of action by alcohol. Examples are given of patients' own accounts and dream-associations which illustrate and confirm the formulations. Study of 2 patients in particular gave direct evidence that the barrier acts as a shield or protection against the world and its pressures. Again, it is associated with a quality of defiance which is the basis for a kind of self-confidence which functions on the theory that the individual can ignore reality or defeat reality any time he really puts his mind to it. And again,

hostility and its associated aggressiveness contribute to the barrier.

Treatment aims at breaching and removing the barrier and bringing about a working relationship between the inner self and reality. The patient must be brought to feel anxiety about his condition for the alcoholic's blandness about his ailment is notorious and is a real block to effective therapy. To feel such anxiety he must face the impersonal pressures of reality. To make him face these pressures the psychiatrist has to overcome the patient's refusal, unwillingness or inability to do so, which arises from deep unconscious elements. The barrier may close up again at any time to block treatment temporarily or permanently.

[Tiebout's general principle undoubtedly supplies an acceptable explanation of the clinical picture and the meaning of chronic alcoholism. He had space only to touch upon the alcoholic's detached attitude to his illness and his record of insensibility to environmental demands, and to his family; these features could supply ample factual evidence in support of the theory.]

Harry Stalker

1987. **The Hang-Over in Relation to the Theory and Treatment of Alcohol Addiction**

G. LOLLI. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] 7, 193–213, Sept., 1946. 8 refs.

" Irrespective of the specific psychological constellations underlying [alcohol] addiction, a [drinking] bout always expresses the alcoholic's unrealistic attempt to master the unbearable tension arising from his neurotic conflicts. In some phases of acute intoxication repressions dissolve and instinctual drives can find a partial, although often distorted, outlet; and when stupor sets in further stimulation, both external and internal, is made ineffective and thus cannot add to the existing tension. When the bout is over a flood of unmastered physical and mental stimuli produces an even greater state of tension with which the mental apparatus of the individual is unable to cope, and which in its origin and symptoms resembles a traumatic neurosis." The result may be another bout.

The psychological symptoms of the hang-over arise from the patient's previous state and from the mechanisms described above. Many are symptoms of tension and excitation. There are often brief and intense spells of physical and mental emotional disturbance, significant as discharge phenomena. Vegetative neuroses (more prolonged somatic disturbances without conscious emotion) are frequent, especially gastric and cardiovascular syndromes; other syndromes are less common but there is hardly a case of hang-over without some sympathetic-parasympathetic imbalance. Often the same vegetative neurosis is in the background during abstinence. " Alcoholics, because of the excessive demands they make on the environment or because the environment does not furnish adequate supplies to their normal demands, often experience the tension due to insufficient gratification of instinctual needs." As a result of the many frustrations to which they are exposed, more or less inhibited hate and aggression often cause circulatory disturbances that are most evident in the hang-over. Apart from the tremor related to permanent damage of the C.N.S. a tremor of the hands and fingers during the hang-over is a sign of persistent anxiety. Insomnia is frequent, usually due to the overwhelming excitation; sleep is often disturbed by involuntary movements and painful dreams. In the early phases of the hang-over the depression of the C.N.S., due to the lingering presence of alcohol, weakens resistances and facilitates abreactions. Facts of emotional significance may be revealed which would be concealed, consciously or unconsciously, during abstinence.

Somatic symptoms not due to psychological causes include thirst, which is only partially caused by increased diuresis and perspiration; there is experimental evidence that it is due to a shift of water from the intracellular to the extracellular spaces, which in its turn is probably due to alcohol affecting the brain centres regulating water metabolism. Headache may result from a variety of somatic causes. Fatigue comes from both emotional tension and physical activity during intoxication. It is increased by insomnia and anorexia and is sometimes accompanied by hypoglycaemia. Some of the vegetative symptoms may be due to the production during intoxication of substances acting selectively on the vegetative nervous system. There may be acute gastritis of local origin, delayed gastric emptying probably of central origin, and moderate enlargement and tenderness of the liver. More severe gastric disturbance, marked prostration, and headache occur when liver damage existed before the bout. The diseases of chronic alcoholism may be aggravated. Epileptic convulsions are seen more often in the hang-over than during intoxication, and may occur in patients who never have seizures at other times. Lesions due to injury should always be looked for.

Medical treatment begins when the doctor accepts the alcoholic as a patient and studies the addiction with him as a biological phenomenon. The first aim is to correct the acute consequences of the bout, by the administration of a combination of a rapidly and a slowly acting barbiturate for sleep; next to control vegetative symptoms with mild sedatives or drugs, especially a combination of atropine, ergotamine tartrate, and a barbiturate. Amphetamine sulphate may be given for fatigue. Proper diet is essential and supplementary vitamins are required in some cases. The choice between in-patient and out-patient treatment is determined by the circumstances of the case. The alcoholic's need for help in the hang-over outweighs his aggressiveness, which, as a reaction to deeply-rooted craving for dependence, often blocks co-operation during sobriety. The aim of psychotherapy at this stage is to restore equilibrium between the controlling forces and the impulses striving for expression —that is, tensions must be lessened and the subject's control over tensions increased. Daily interviews may be required until the end of the hang-over. Later the patient's attention is focused on his actual environmental problems. Adequate handling of the hang-over leads to permanent sobriety in a few cases, to a definite improvement in many others, and provides a basis for later treatment. A number of cases are quoted to illustrate specific points. *Harry Stalker*

1988. **Attitudes and Learning: A Methodological Note**
D. KRECH. *Psychological Review* [*Psychol. Rev.*] **53**, 290–293, Sept., 1946. 5 refs.

In the rat the learning to solve problems should not be regarded as the result of random responses. Faced with a problem the rat brings to bear a whole history of experiences and goes about his task in an orderly systematic manner. This conception is compatible with both the molecular and molar theories of learning. This approach seems to be useful in the study of human attitudes which have been very differently interpreted according to whether they have been studied from the molecular or molar point of view. The author suggests that in fact most people have attitudes towards problems or situations which are not imposed on them *ab extra* by propaganda conditioning or coercion, but are developed because of the needs of their personalities and the requirements of the situation (the molar approach). One of the functions of attitudes is to integrate social perceptions and experiences. These attitudes, which correspond to McDougall's sentiments, change, grow, and wane throughout life. They are attempts by the individual to solve some of the problems confronting him in his social world, and are therefore not influenced by learning, but are the very stuff of learning, at least in one social segment of the individual's personality. By means of attitudes, specific new social phenomena can be organized and dealt with more efficiently, and by adopting an attitude to certain things it may be easier to deal with and solve certain other social, economic, or political problems. Nevertheless, attitudes are not always adopted consciously, and still less are they adopted consciously as a means to achieve a more comprehensive knowledge of, or power of dealing with, wider issues. A study of the history of attitudes may show that, like the learning of rats, they are not the result of trial-and-error hit-and-miss associations, but that they display an organized development and represent a meaningful part of a person's total behaviour. By the development of his attitudes a man's personality is built up into an organized whole, which is not a " chaotic, senseless, irrational aggregate of stereotypes, prejudices, biases, and conditioned responses fortuitously acquired ". *R. G. Gordon*

1989. **Personality Studies in Menopausal Women**
K. STERN and M. PRADOS. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **103**, 358–368, Nov., 1946. 3 figs., 29 refs.

In a review of the literature on psychological concomitants of the menopause such symptoms as " convulsions of the stomach ", melancholia, anxiety, prickling and burning of the skin of the limbs, pseudo-narcotism, uncertain gait, insomnia, migraine, and hallucinations are mentioned. Shorr believed these disturbances to be exacerbations of previously existing trouble, while Merson, in a study of admissions to a mental hospital, noted a marked relationship between the menopause, home troubles, and psychoses. Fatigue, curiosity, and suggestion also seem to play a part in the causation of symptoms.

In the present study 23 of 50 women with the menopausal " syndrome " had undergone an artificial menopause, 22 by surgical intervention. All the patients were poor, and most had attended out-patient departments with menopausal symptoms for a considerable period before the study was made. In all of them hot flushes were noted and 41 complained of depression. In 20 cases there were headaches, in 20 there was abdominal discomfort, in 16 a feeling of tension, and in 7 backache. Other symptoms were abnormal sensations in the limbs (9), nausea (4), palpitations (6), pruritus (4), cranial nerve and breast symptoms, and attacks of unconsciousness. Marital difficulties appeared to be a very common concomitant of depression. There was high blood pressure in 8 of the 50 patients. *Beryl Twyman*

1990. **Group Psychotherapy with Veterans**
N. W. ACKERMAN. *Mental Hygiene* [*Ment. Hyg., N.Y.*] **30**, 559–570, Oct., 1946.

Group psychotherapy is not a substitute for individual psychotherapy, though the two may be used together. Three questions about group therapy require to be answered: (1) How far is it an experience in social re-education? It would seem to have definite benefit in this respect. (2) What is its therapeutic value and in what cases is it useful? It is useful in mild cases in which the patients require the support of the group to overcome their feeling of inferiority or who are repressing aggressive feelings against society or individuals in their family circle. (3) How economical is the method? It certainly takes less time than individual therapy and therefore when successful is economical. It is not suited to cases with serious intrapsychic distortions.

Groups were mostly composed of cases of social maladaptation with marked reactive anxiety, mild character disorders, true combat neuroses, and mild psychosomatic manifestations. Before admission to the group each man underwent medical and psychological examination, and psychometric and vocational tests were given when necessary. The size of the group was restricted to 7 members who met once a week for 1½ hours. Verbatim notes were taken of 35 sessions. The men were encouraged to talk freely and discuss their difficulties, symptoms, and phantasies. The aims were: (1) to provide emotional support through group relationships; (2) to activate emotional release especially of aggression; (3) to reduce guilt and anxiety; (4) to test various forms of social reality in this group; (5) to increase self esteem and tolerance of others; and (6) to increase insight into the meaning of symptoms. Details of 4 cases are given to illustrate how these aims are achieved. Such group therapy certainly has a place for selected cases in both military and civilian communities. *R. G. Gordon*

1991. **Bilateral Frontal Lobe Leucotomy in the Treatment of Mental Disease**
K. G. MCKENZIE and L. D. PROCTOR. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **55**, 433–441, Nov., 1946. 8 figs., 14 refs.

Infectious Diseases

VIRUS INFECTIONS

1992. **Growth of Japanese B Encephalitic Virus in the Yolk of the Developing Egg**
B. F. HOWITT. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **62**, 105–108, June, 1946. 6 refs.

This work was undertaken to determine the possibility of using infected chick-embryo tissues or fluids for making a vaccine against the Japanese B virus. Fertile hens' eggs were inoculated by either the allantoic or yolk-sac routes and the presence of virus was estimated by intracerebral inoculation of Swiss mice. The original inoculum was a 10% mouse-brain suspension (titre $10^{-8\cdot3}$). Embryonated eggs 10 to 11 days old were inoculated with 0·2 ml. through the air-sac membrane into the allantoic fluid. The optimum titre—$10^{-6\cdot0}$ to $10^{-7\cdot5}$—was obtained after 3 days' incubation, at which time most of the embryos were still alive. Thirteen passages of 0·2 ml. of a 10% suspension of embryo and chorio-allantoic membrane in buffered saline failed to produce any increase in virulence. The titre remained constant and the lethal effect inconstant. Incubation at 95° C. gave better results than incubation at 98° C. When the yolk-sac route was tried 0·2 ml. of a 20% mouse-brain suspension (titre $10^{-8\cdot5}$) was injected into 8-day-old embryos and resulted in 100% mortality in 48 hours. This method may be used for titration of virus. Further investigation showed that the maximum titre was obtained after 36 hours' incubation at 95° C. Pooled embryos and chorio-allantoic membranes from 7-, 8-, and 9-day-old embryos all gave the same titre, but 15-day-old embryos survived for 72 hours and contained less virus. There was less virus in yolk sacs at all ages. The titre of the virus in the eggs increased with increase in virus in the inoculum, but never reached the maximum titre of the mouse-brain suspension. Passage by the yolk-sac route did not increase the virulence for egg. The use of normal rabbit serum as diluent instead of buffered normal saline did not yield any increase in potency.

F. O. MacCallum

1993. **Effect of Time of Contact at 37° C. and Hydrogen Ion Concentration on the Degree of Neutralization of Equine Encephalomyelitis Virus (Eastern Type) by Immune Serum**
N. A. LABZOFFSKY. *Journal of Infectious Diseases* [*J. infect. Dis.*] **79**, 63–68, July–Aug., 1946. 8 refs.

Previous reports in the literature on the *in vitro* interaction of equine encephalomyelitis virus and specific antiserum have not been in complete agreement. The virus studied in this work was the Eastern type isolated from an infected horse in Ontario in 1938; it was used in the form of infected chick-embryo tissue. The immune serum was obtained from guinea-pigs. In the first series of experiments the effect of time of contact on the degree of neutralization was investigated. In the second series the effect of *p*H was examined. In both a given quantity of virus was mixed with an equal volume of serum dilution. These mixtures were then distributed in 1 ml.-ampoules and sealed; several ampoules were filled with each mixture, and all were incubated at 37° C. Thereafter 10-fold dilutions were made, and titrated for infectivity in Swiss mice, 3 to 4 weeks old, by the intracerebral route.

It was found that with increased time of contact there was a progressive decrease in the infectivity of the serum-virus mixtures. In a representative experiment this decrease continued up to about the twenty-fifth hour, no further reduction being observed thereafter. The number of hours required for the reaction to reach completion depended on the concentration of the constituents used in the test. In another experiment it was shown that, provided the virus and serum were in contact for 28 hours at 37° C., the inactivating property of the serum was the same whether the virus and serum were mixed before or after dilution. Variation in hydrogen ion concentration between *p*H 5·6 and 8·2 did not appear to influence the degree of neutralization obtained after virus and serum were held in contact for 24 hours at 37° C.

These observations suggest that the virus of equine encephalomyelitis (Eastern type) interacts *in vitro* with its specific immune body. No dissociation occurred on dilution of virus–serum mixtures, indicating that the reaction is of a stable and irreversible character.

A. J. Rhodes

1994. **Modification of Human Red Cells by Virus Action. I. The Receptor Gradient for Virus Action in Human Red Cells**
F. M. BURNET, J. F. MCCREA, and J. D. STONE. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **27**, 228–236, Aug., 1946. 2 figs., 7 refs.

It has been shown that red cells agglutinated by Newcastle disease virus (N.D.V.) develop resistance to subsequent agglutination by that virus, while remaining susceptible to agglutination by the influenza viruses. Furthermore, the viruses of this group can be arranged in a series such that cells rendered resistant by treatment with a given virus fail to be agglutinated by virus strains earlier in the series, but are still agglutinated by those succeeding it. In the present paper the authors have extended this work, and describe a similar receptor gradient in human red cells for a wide range of viruses of this group. It is further shown that human erythrocytes treated by viruses of this group, in addition to losing their agglutinability by some or all of these viruses develop a susceptibility to serum agglutination analogous to the "panagglutinability" described by Thomsen. The titre obtained with normal human serum is roughly

proportional to the position in the receptor gradient of the virus used to prepare the cells.

Further experiments demonstrate the ability of two different types of bacterial products to alter in a like manner the character of human red cells so that they become progressively less sensitive to agglutination by viruses. *Clostridium welchii* toxin type A and *Vibrio cholerae* filtrates are capable of bringing about this change, and the fact that both organisms produce an active lecithinase suggests that this enzyme may possibly be concerned in the phenomenon. There is, however, evidence to suggest that this phenomenon cannot be directly correlated with that of the virus receptor gradient. Mumps virus receptors are more readily removed by virus action than by vibrio filtrates; virus receptors may be almost completely removed by vibrio filtrates with little development of serum agglutinability; and finally panagglutinability is consistently produced by Friedenrich's strain M, a diphtheroid, without loss of virus receptors. The authors conclude that, with regard to haemagglutination, viruses may exert their action by virtue of an enzyme or enzymes, which may also play an essential part in the initial invasion of susceptible cells. It is proposed to direct further work toward the characterization of the enzyme or enzymes responsible for these effects. *A. Henderson-Begg*

1995. **Modification of Human Red Cells by Virus Action. II. Agglutination of Modified Human Red Cells by Sera from Cases of Infectious Mononucleosis**

F. M. BURNET and S. G. ANDERSON. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **27**, 236–244, Aug., 1946. 1 fig., 10 refs.

During the investigation described in the first paper of this series (see Abstract 1994) it was observed that serum from a patient with infectious mononucleosis agglutinated cells treated with the virus of Newcastle disease of fowls to a titre of 1 in 15,000. This virus is one of the earliest of the series described in the foregoing paper, and it might thus be expected that N.D.V.-treated cells would give a low panagglutination titre with a normal serum. The virus of Newcastle disease of fowls is shown to agglutinate human cells and be eluted from them in the same manner as in the case of influenza viruses lower in the series. Human cells previously treated with N.D.V. (amniotic or allantoic fluid preparations) are shown to be agglutinated to high titre by specific immune sera prepared in fowls, guinea-pigs, or rabbits, and to lower but still considerable titres by sera from animals inoculated with other viruses.

Of about 70 normal human sera, mostly obtained in connexion with influenza investigations and tested against human cells treated with N.D.V., the majority showed some agglutinating power, but titres were all below 1 in 120, and no significant variations were evident in pairs of acute and convalescent sera from patients with influenza. On the other hand, 7 out of 13 sera from cases of infectious mononucleosis, in which the diagnosis was regarded as clinically and haematologically reasonably certain, and in which the Paul-Bunnell reaction was positive (titre of 1 in 200 or over) showed agglutination of N.D.V.-treated cells to a higher titre than normal. Of the remaining 6 cases where the Paul-Bunnell response was below a diagnostic level, 2 agglutinated N.D.V. cells to a significant level. The antibody responsible for this reaction acts only on cells treated with N.D.V., and not on cells treated with other viruses of the group, and in this way differs from that concerned in the agglutination of N.D.V.-treated cells by normal human sera. Experimental investigation of the cell sensitizing agent shown to be present in N.D.V. preparations demonstrates that it can be clearly differentiated from the virus particle itself. If, after the agglutination of human red cells with infectious mononucleosis serum, the supernatant fluid containing eluted virus is treated successively with fresh cells, its sensitizing power diminishes sharply while the virus titre falls much more gradually. Similarly it can be shown that virus eluted from washed cells has no power to sensitize fresh cells.

The authors discuss this phenomenon and suggest three possible explanations. First, the aetiological agent may be a virus antigenically related to N.D.V. Secondly, the relationship between antibody and sensitized cells may be due essentially to an accidental resemblance of antigenic structure. Thirdly, the development of a labile globulin which reacts strongly with both N.D.V. and sheep cell antigens may occur during the course of infectious mononucleosis. The activity of the globulin on this view would not be a manifestation of specific immunological modification in response to a micro-organism as antigen. *A. Henderson-Begg*

1996. **Colorado Tick Fever**

L. FLORIO and E. R. MUGRAGE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **25**, 466–472, Sept., 1946. 3 figs., 8 refs.

In 1930 Becker gave the name Colorado tick fever to a disease syndrome which had previously been regarded as a mild form of Rocky Mountain spotted fever, following the observation that blood from cases of the disease failed to evoke symptoms or the characteristic scrotal reaction in guinea-pigs. The disease, which is always accompanied by a history of exposure to tick bites 4 to 6 days before the sudden onset, is characterized by pyrexia, generalized aching, headache, deep ocular pain, and lumbar backache, with photophobia, anorexia, and nausea. The temperature falls in 2 to 5 days, and after a symptom-free remission of an approximately similar period, there is a second attack which may last for slightly longer than the first. Neither rash nor complications have been noted. The white blood-cell count falls to between 2,000 and 3,000 per c.mm.; all types of white cells are affected, except the monocytes. There is a well-marked shift to the left in the granulocytes.

The authors have investigated the possible relationship of this disease to Rocky Mountain spotted fever and dengue, which it closely resembles both clinically and haematologically. Typical Colorado tick fever was reproduced in human volunteers by the subcutaneous inoculation of sera from naturally occurring cases, and three convalescent volunteers proved immune to

subsequent reinfection 9 to 12 months after the original infection. Volunteers immunized against Rocky Mountain spotted fever were susceptible to infection with Colorado tick fever one month after the last dose of tick vaccine. Similarly, Colorado tick fever was induced in human subjects convalescent from dengue. Golden hamsters proved susceptible to inoculation with sera from cases of Colorado tick fever; a leucopenia developed and there were alterations in the cellular type and arrangement of the follicular lymphoid tissue of the spleen. After the seventh transfer, serum produced the typical disease in a human being. Beyond the twelfth passage these findings were accompanied by a 25 to 50% mortality in the animals. Serum from a normal hamster failed to elicit similar pathological findings after 10 serial passages of pooled sera, and likewise failed to reproduce the disease in volunteers. The infecting agent was not visualized throughout these experiments, and could not be grown on laboratory media, or in the chick embryo. It was found to pass a 24mμ membrane, though such filtrates were only capable of infecting man after hamster passage. It resisted freeze-drying, and survived for 3½ years at 0° C.

The authors conclude that the infecting agent of Colorado tick fever is an extremely small virus comparable in size to that of poliomyelitis and yellow fever. The evidence for tick transmission of the disease is at present entirely circumstantial. *A. Henderson-Begg*

1997. **Attempts to Adapt Murine Poliomyelitis Virus to the Chick**

P. BRUTSAERT, C. W. JUNGEBLUT, and A. KNOX. *Journal of Pediatrics* [*J. Pediat.*] **29**, 350–355, Sept., 1946. 2 figs., 10 refs.

A strain of rodent-adapted poliomyelitis virus (MM) was tested for its infectivity by the allantoic route in embryonated eggs. The strain could not be recovered after five or six serial passages. Chicks injected intracerebrally harboured virus, and developed serum antibodies, but no definite adaptation to this species could be demonstrated. *A. J. Rhodes*

1998. **Tenth Report on Data of Anti-Rabies Treatments Supplied by Pasteur Institutes**

M. GREENWOOD. *Bulletin of the Health Organization* [*Bull. Hlth Org., L. o. N.*] **12**, 301–364, Oct., 1946. 15 refs.

After a recommendation by the International Rabies Commission of 1927 the Health Organization of the League of Nations was invited to publish statistics of the results of anti-rabies treatments from annual reports furnished by every Pasteur Institute. Nine successive reviews were subsequently published of the data collected up to 1937; the present author undertook to produce the tenth and final report, and has submitted the analysis of the final set of data, which refers mainly to the years 1938 and 1939, together with the aggregates for all ten reviews, in the same form as that adopted by his predecessor in the earlier reviews.

The cases available for the tenth review consist of 228,051 treated patients, bringing the total for all ten reviews combined to 1,290,758; among these the deaths recorded numbered 483 and 4,024 respectively—mortalities corresponding to 0·21% and 0·31%. Not included in these figures are data supplied by Russia for the years 1927 to 1937, which bring the total number of treated persons to 1,670,848, with a mortality rate of 0·28%.

Throughout the review the methods of treatment have been classified as follows:

1. Dried and glycerinated cords (Pasteur's original method and Calmette's modification).
2. Modified dilution method (Högyes).
3. Killed phenol vaccines (Semple and Mulford's modifications).
4. Live phenol vaccine (Puntoni's method).
5. Fermi's original vaccine.
6. Fermi's serovaccine.
7. Heated vaccines (Babes).
8. Killed ether vaccine.
9. Mixed treatments:
   (*a*) Dilutions plus Alivisatos's etherized vaccines.
   (*b*) Dried cords plus, in severe cases, Fermi's original vaccine.
   (*c*) Fermi's vaccine plus, in severe cases, Alivisatos.
10. Yatren vaccine.

For certain tabulations in the analysis these ten methods have been grouped into a short classification: (1) killed vaccines comprising 3 to 8 above; (2) live vaccines comprising 1, 2, 4, 9 (*a*) and (*b*) above; (3) heated vaccines comprising 7 above; and (4) other treatments comprising 5, 6, 9 (*c*), and 10 above. This shorter classification has been used for certain tabulations from the fourth review onwards, but it is possibly more reasonable to combine all the phenol vaccines into one group irrespective of their degree of attenuation. A detailed table is given showing the distribution of cases (228,051) included in the tenth review, and their mortality by institute and year of treatment and, where possible, the dosage, duration, and type of treatment adopted. This detail is further summarized together with the data for all reviews combined, to show the numbers of patients treated and mortality for each type of treatment.

The main analysis shows the number of patients treated, the number of deaths occurring, and the mortality rates for each type of treatment for the data dealt with in the tenth review alone. For the data of all ten reviews combined each of the following variables is analysed: (1) Race of patient—in terms of European or non-European; (2) species of biting animal; (3) evidence of rabies in biting animal; (4) severity of bite; (5) intervention of clothing; (6) position of bite; and (7) delay in beginning treatment. The tables referring to the last five variables are further subdivided between Europeans and non-Europeans. The presentation concludes with an analysis of paralytic accidents and their fatality according to type of treatment.

Statistical analysis has been carried out by means of the χ^2 test, the technique of which is described. In the interpretation of the results the author emphasizes: (1) the lack of homogeneity of place and time inherent in the data; (2) the fact that their reliability is largely dependent upon the completeness of the "follow-up" technique employed by the various institutes concerned;

and (3) the possibility of variations occurring in the infectivity of strains of rabies viruses between time and place. All these possible causes of heterogeneity would affect comparisons made between groups, for although the number of treated persons is large, the absolute number of deaths is very small. It is demonstrated that over a period of time, within one method of treatment, there occurs a change in the rates of mortality; this makes comparisons between treatments somewhat difficult in terms of the aggregate results of 10 years, and the author states that " as a statistician I do not feel able to deduce from the data here assembled any result which would entitle me to conclude that any one of the prophylactic methods compared has such a superiority over other methods that a jury of reasonable men would recommend its universal application ". The earlier work of van Stockhum, who advocated a rather different statistical approach to the problem, basing the analysis on actual deaths, is reviewed by the present author, and her methods are examined by use of the League of Nations' data. *E. A. Cheeseman*

RICKETTSIAL INFECTIONS

1999. **The Complement-Fixation and Weil-Felix Reactions in a Study of Typhus Among Wild Rats**
A. POMALES LEBRON, G. ARBONA, P. MORALES OTERO, and E. KOPPISCH. *Puerto Rico Journal of Public Health and Tropical Medicine* [*Puerto Rico J. publ. Hlth*] **21**, 350–356, June, 1946. 5 refs.

A report is given of a serological study of wild rats trapped in the city of San Juan, Puerto Rico, between December, 1944, and June, 1945. Complement-fixation tests were performed with epidemic typhus antigen prepared by the technique described by Bengston (*Publ. Hlth Rep., Wash.*, 1944, **59**). Of 413 sera examined 54% gave positive reactions. Classification of the animals according to size, species, and sex showed that a significantly higher proportion of large, older rats gave positive complement-fixation reactions, whereas with regard to species and sex no difference was observed. Rats trapped in the same localities at different times of the year showed no significant difference between the proportions of positive reactors. This finding was in marked contrast to the existing fluctuation in the number of cases of typhus reported for the same periods. Differences were observed, however, in the proportion of positive reactors to the complement-fixation test among animals trapped in different sections of the city and during different months.

Complement-fixation and Weil-Felix tests were carried out in parallel on 251 sera. Of these 139 gave positive complement-fixation and 61 (24%) positive Weil-Felix reactions. In the positive complement-fixation group, 42 (30%) were also Weil-Felix-positive, and in the complement-fixation-negative group 19 (17%) were positive Weil-Felix reactors. Alcohol-treated suspensions of *Proteus* OX19 were employed in this study, and the authors attribute the wide variations in the results reported by different workers with the Weil-Felix reaction in wild rats to differences in the nature of the suspensions and susceptibility to agglutination of the OX19 strains employed, and to differences in the methods of reading and recording results. The results of this investigation showed a marked lack of correlation between the complement-fixation and Weil-Felix reactions; the authors suggest that the latter reaction may be of as fleeting a nature in wild rats infected under natural conditions as it has been demonstrated to be in experimentally-infected rats.

A. Henderson-Begg

2000. **Serological Relationships in the Epidemic-Endemic Typhus Group as Determined by Complement Fixation**
I. A. BENGTSON. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **61**, 1379–1385, Sept. 20, 1946. 3 refs.

A serological study was made of 16 strains of epidemic and 3 of endemic typhus by complement-fixation tests. All strains were cultivated in the yolk sacs of chick embryos, and the antigens prepared by a modification of Craigie's ether extraction method. Sera obtained from convalescent guinea-pigs which had been bled 2 to 3 weeks after the subsidence of fever were tested against a fixed amount of each antigen, determined by previous titration against a fixed dilution of a moderately high titre homologous serum. The results indicated a serological similarity among all the epidemic typhus strains, and also among the three endemic strains studied. Differentiation between epidemic and endemic typhus was shown by higher titres against the homologous than against the heterologous strains.

A. Henderson-Begg

2001. **The Distribution of the Pathologic Lesions of the Central Nervous System in Scrub Typhus (Tsutsugamushi Disease)**
A. WEIL and W. HAYMAKER. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **5**, 271–284, Oct., 1946. 14 figs., 5 refs.

The authors investigated the entire nervous system in 21 cases of scrub typhus originating in New Guinea. The duration of the illness varied from 8 to 31 days. The staining systems employed were limited to haematoxylin and eosin, cresyl violet, and silver methods. The intensity of the lesions varied, but their distribution was more or less constant, the leptomeningeal reaction being most marked over the upper parts of the convex and medial surfaces of the brain and in the region of the rhinal fissure and subcallosal gyrus. In the parenchyma the perivascular reaction was most pronounced in the periventricular region, the corpus striatum, and the amygdalo-hippocampal complex. Glial and mesenchymal " nodules ", usually perivascular in distribution, were about twice as frequent in the grey as in the white matter. Neurone necrosis with neuronophagia, such as occurs in epidemic encephalitis, was not observed.

R. M. Stewar

2002. **Inoculation Experiments Against Typhus in Afghanistan**
Z. BERKE. *British Medical Journal* [*Brit. med. J.*] **2**, 944–945, Dec. 21, 1946.

Typhus is endemic in and around Kabul. Cases are sporadic in the summer but become more frequent in the autumn; the disease is most prevalent during the winter. Season has no marked effect upon clinical severity; very severe cases, many without rashes and therefore to be diagnosed only by serological methods, may occur in the early summer. It was found, however, that the serum of patients suffering from typhus might fail to agglutinate suspensions of *Proteus* OX19 but did agglutinate one or both of the variant strains (or types) OX2 and OXK, and that such cases tended to occur in the spring and autumn. The Weil-Felix reactions in 123 sera positive for one, two, or three types were as follows:

Proteus	*Positive*	*Negative*
OX19	116	7
OX2	73	50
OXK	33	90

It is therefore the rule at the Institute of Bacteriology at Kabul to carry out the Weil-Felix test with all three types, and although the serum may contain agglutinins to all three, the titres differ; one is the main type and the others are coagglutinins.

For the protection of civilian prisoners the author prepared a vaccine from the blood (W.F.R. positive and Kahn negative) of patients taken during the second week of a severe attack of typhus. The blood was defibrinated and filtered; phenol or formalin was added and the blood kept at 56° C. for 1 hour. After checks for sterility the vaccine was stored in the refrigerator and warmed to blood-heat before use. Three weekly injections (2, 4, and 4 ml.) were made into the subcutaneous tissue of the abdominal wall. Among a first batch of 2,196 prisoners exposed to typhus in gaol there were no cases during the first 6 months and only 9 in the ensuing 2 months, of which 2 were fatal. Among a second batch of 368 prisoners 13 cases occurred of which 2 (both in feeble persons) were fatal. Of 110 uninoculated prisoners with typhus 89 recovered and 21 died. Protection was valid for from 5 to 6 months. The author, like other observers, also reports very favourably upon Cox's vaccine. In 1943, 3,122 persons were inoculated with American typhus vaccine (Cox type). The outbreak during that year was not serious, but cases and deaths were recorded among the uninoculated, whereas among the inoculated there were only mild cases with no deaths. *E. H. R. Harries*

TUBERCULOSIS

2003. **Employment of Ex-Tuberculous Patients**
H. S. WILLIS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 9–12, July, 1946. 2 refs.

The author pleads for the employment of ex-tuberculous patients in sanatoria and hospitals, contending that no increased liability to illness attends this practice. In support of this statement he quotes the experience of the Maybury Sanatorium, Detroit, where occasionally ex-tuberculous patients have been employed. The sanatorium has 845 beds and normally employs 561 persons, 88 of whom have had tuberculosis previously. These 88 people included physicians, nurses, clerical workers, attendants, orderlies, laundry workers, plumbers, and messengers, who had worked altogether 559 man-years. Collectively they had lost 10 man-years from tuberculosis.

To dispel the belief that this group of ex-patients was more than usually liable to absenteeism from conditions other than tuberculosis the author consulted the records of 58 of them, covering 152 man-years, or an average of 2·6 man-years each, and found a total loss of 1,527 days' work, or 10 days per person per year. This was compared with the record of 100 able-bodied employees (every fifth person who had worked a year or more was chosen), who were found to have lost 2,300 days from non-tuberculous ill-health, or 9·4 days per person per year. The records also showed that 26 employees who had no sign of tuberculosis on entry developed the disease while at work and between them had spent 30 years in hospital in consequence. " Thus three times as much absenteeism was experienced by 26 people who contracted tuberculosis while at work as was lost by the 88 employed ex-patients." This conclusion was deduced without any relation to the total number of employees involved or the number of years worked. The author admits the weakness of this when he adds that " those ratios are . . . only suggestive, because the numbers of able-bodied employees who did not develop tuberculosis are unknown but large ". The group of 88 ex-patients proved more stable than the average, with less turnover; 40 are still working in the sanatorium, while many of the remainder have left to seek posts elsewhere.

In selecting suitable patients for work in the sanatorium the author pays attention to the type of tuberculosis they have had, with special reference to any previous relapses, and the type of work they will be called upon to do. He recommends a three-month " hardening " process at home, with gradually increasing exercise followed by a full review. If satisfactory the patient is employed half-time for 3 months. " Every State has a reservoir of such good-risk people who could be reckoned as suitable for average hospital work."

[The author's figures of the relative risk of absenteeism from tuberculosis in the two groups may lead to a false impression, and it would be unwise to assume from them that the total time lost by fresh cases occurring in the able-bodied would be three times that lost by relapses in a staff wholly composed of ex-patients. The data are insufficient for such a calculation. The ratio might quite easily be the other way round, and experience with mass radiographic surveys suggests that it would be. But the problem is not a mathematical or even entirely an economic one; it is largely one of therapeutic rehabilitation. The environment and amenities of the sanatorium are frequently ideal for the person with arrested or quiescent tuberculosis, and the author is probably right when he says that better work is often obtained from these than from the healthy. Certainly

in Great Britain those who have tried the experiment have so far no reason to be displeased.]

N. Lloyd Rusby

2004. **Patients' Information about Tuberculosis. A Survey with a Standardized Questionnaire**
J. NEWMAN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 13–24, July, 1946. 9 refs.

Newman quotes Parran (*Amer. Rev. Tuberc.*, 1944, **50**, 365) as saying of tuberculosis control that it " was the first instance in which we undertook to control a disease, not by specific immunization or quarantine, but essentially by the power of public education ". Deeming such education to be an individual matter, with allowance to be made for a difference in intelligence, background, and personality factors, the author set out to discover how much a patient already knows, as a preliminary to deciding in which direction educational efforts could best be launched. He accordingly devised a comprehensive questionary, which he submitted to four groups of people: (1) new patients in a sanatorium (95); (2) old patients who had been in the institution for some time (111); (3) 50 " experts " composed of tuberculosis workers of all kinds, a group largely used as a test of ambiguity in the questions; (4) 178 students in one of the New York City Colleges, representing a " selected portion of the general population " and considered to be superior to the average intellectually.

It is not possible to tabulate all the results, and the paper should be consulted by anyone planning an educational programme for patients, but the following is a short summary of the more important. The points generally understood by the various groups were: contagiousness is a factor to be considered; tuberculosis is not inherited; the disease is not fatal; rest is an important part of treatment; each case of tuberculosis is different; a sanatorium treatment is valuable; and follow-up care after discharge and hygienic measures in the home are necessary. It was less generally understood that *x*-ray examination is the best diagnostic procedure. There was improved understanding among the old patients after a period of sanatorium treatment of the specific means of acquiring tuberculosis and the viability of tuberculous germs; that overweight is of no value, and outdoor work is not advisable; that it is helpful to plan for the future while still a patient, and that it is inadvisable to judge progress by subjective feelings of good health. Generally all groups failed to understand that tuberculosis may run an erratic course, and that disinfection of sputum must be radical. They did not recognize the subtle symptoms of tuberculosis or the significance of negative sputum in relation to progress.

N. Lloyd Rusby

2005. **Results of Pneumonolysis**
H. MARCUS and M. PINNER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 25–40, July, 1946. 4 refs.

The authors have followed up 302 consecutive patients submitted to pneumonolysis during treatment for pulmonary tuberculosis between 1937–43 at the Montefiore Hospital, New York. In 13 the pneumothorax was bilateral; the total number of pneumothoraces, therefore, was 315. In all, 401 operations were performed on these 302 patients. The observation period in all but 42 (13·9%) was from 2 to more than 6 years. The disease was moderately advanced in 80 patients, and far advanced in 222. There were no minimal cases in the series.

For convenience of analysis the pneumothoraces were divided into four groups: group 1 in which all adhesions attached to diseased lung tissue were divided, thus giving complete pneumonolysis (88 cases); group 2, partial pneumonolysis, in which key adhesions were cut completely or in part, but some adhesions or parts of adhesions were left intact (102 cases); group 3, insignificant pneumonolysis, in which some adhesions were cut but key adhesions could not be severed (24 cases); and group 4, thoracoscopy only, in which either no adhesions were seen (3 cases) or none could be cut (98 cases). In all groups the total percentage of favourable results directly attributable to the operation was 40, the percentage figures in each group being 54·5, 47·1, 37·5, and 20·8 respectively. The percentage of good results achieved after further sanatorium treatment with additional collapse therapy was 79·7 for all groups. The individual percentage figures for each of the four groups show a relatively close approximation, being, from groups one to four, 87·4, 79·5, 70·8, and 75·3. Of particular interest in this connexion is the behaviour of group four in which only inspection of the pleural cavity was carried out. In no less than 20·8% of these 101 pneumothoraces improvement resulted sufficiently soon after operation for the authors to attribute it to the procedure; a further 54·5% improved after additional treatment which included thoracoplasty in 8 patients. [That a group of patients in which no adhesions would be divided should in the end fare nearly as well as those in which all adhesions were cut is unexpected. This raises a question of the highest importance concerning the management of this class of case.]

The complications met with were those usually recorded. Transitory effusions were seen after 45·9% of operations; their incidence varied with the extent of the intervention. Haemothorax resulted 7 times and was twice followed by obliterative pleurisy: all these patients did well except one who was also suffering from sprue. Massive persistent effusion, which on 3 occasions became purulent, occurred after 4·2% of the operations. Empyema occurred 16 times, and was due to tuberculosis in 7 cases (5 in group two, 1 each in groups one and four), mixed infection in 8 (4 each in groups one and two), and staphylococci in 1 (group one). " All but one empyema, and all but one death, occurred following complete or partial pneumonolysis . . . One gains the impression from a review of the literature that the most dangerous type of operation is the one in which adhesions are partially cut ". After 128 operations in the period 1937–9 the incidence of empyema was 8·6%, whereas in 1940–3 after 273 operations the incidence was only 1·8%. The authors ascribe this difference to a better selection of cases for pneumothorax and to an improvement in the skill and experience of the surgeon.

The incidence of empyema was compared with its incidence in 78 cases in which pneumothorax was alone induced. Empyema was three times more common with simple pneumothorax. [This supports the view of other workers that pneumonolysis prevents empyema more often than it causes it.] Ten deaths were directly attributable to operation, 4 in the first six months after operation (2 in group one and 2 in group two) and 6 later (1 each in groups one and four and 4 in group two).

[This paper, with its 16 tables, does not readily lend itself to abstraction. Moreover, confusion is apt to result from the figures referring in some cases to the number of patients and in others to the number of pneumothoraces. Although the series is small it repays study.] *N. Lloyd Rusby*

2006. **Cultures of Pulmonary Secretions—their Accuracy in the Evaluation of Activity in Pulmonary Tuberculosis**
L. L. SANFORD. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 67–73, July, 1946. 1 ref.

The author's material consists of all the patients admitted to the Muirdale Sanatorium (Wisconsin) for the 5-year period Jan. 1, 1940, to Jan. 1, 1945. " Of the 2,126 adult patients, tubercle bacilli were demonstrated in 1,641 and not demonstrated in 411. Seventy-four patients considered to have had inadequate laboratory studies were not classified. . . . The period of study required to demonstrate tubercle bacilli varied from a few days to two and one-half or even three months." Direct smears and concentrates were negative in 29% of 1,641 adult patients. A total of 4,652 examinations made on 273 patients included 20 examinations of direct smears from sputum; 928 of concentrates; and 12 of guinea-pig inoculations; the remaining examination material consisted of 1,291 concentrates of gastric contents, 1,278 cultures, and 136 guinea-pig inoculations; specimens were collected by bronchoscopic aspiration and examined, 1 by direct smear, 33 by concentrates, and 33 by culture. Of 105 patients with minimal pulmonary lesions encountered in the positive group, 78 were first found positive by culture. In other words, direct smears and concentrates failed to demonstrate tubercle bacilli in 70%. In these, 55 were never positive by any method except culture. Nine additional ones were positive by both guinea-pig inoculation and culture, but by no other method.

On correlating the number of patients who died and the type of investigation used to discover tubercle bacilli in the pulmonary secretions, it was found that 46% of deaths had occurred in the group found positive by direct smear of the sputum, while only 4% were in the group first found positive by culture of the gastric contents. " If we assume mortality to be an index of the extent of the disease or the severity of the pathological process, it seems logical to believe that culture methods, as compared to smears or concentrates, are more capable of demonstrating tubercle bacilli in the less severe pathological processes."

The 408 negative cases were grouped as follows: non-tuberculous pulmonary lesions, 173; no pulmonary lesions, 38; pleurisy with effusion, 19; and pulmonary tuberculosis, 178. Most attention was naturally paid to the 178 patients with pulmonary tuberculosis and their number was finally reduced to 16. These 16 gave a positive reaction to the tuberculin skin test and the radiographs showed some degree of exudative disease, but their sputum cultures were always negative. Thus a group of 16 patients (less than 1% of the 1,657 active adult patients) had, presumably, active pulmonary tuberculosis, and not only direct smears and concentrates, but also cultures failed to demonstrate tubercle bacilli. This result is shown in the following table of relative efficiency.

Procedures	Effective in	Efficiency %
Direct smears ..	923 of 1,657 patients	55
Concentrates ..	1,368 of 1,657 patients	82
Cultures and guinea-pig inoculations ..	1,641 of 1,657 patients	99

It is of interest to compare these findings in adults with those for the group of 126 children examined. This is shown for 43 of them in the following table:

Procedures	Effective in	Efficiency %
Direct smears ..	3 of 43 patients	7
Concentrates ..	7 of 43 patients	16
Cultures and guinea-pig inoculations ..	30 of 43 patients	69

It is worth noting that 7 children had pleurisy with effusion with no visible pulmonary infiltration. Of these, 2 were shown to have tubercle bacilli in their gastric contents. It is concluded that " deaths in the sanatorium were almost twelve times as frequent in patients first found positive by direct smear of their sputa as those first found positive by culture of their gastric contents ".

S. Lyle Cummins

2007. **Investigation of the So-called Primary Abdominal Tuberculosis. Preliminary Report**
S. S. MISRA. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] **15**, 334–336 and 328, July, 1946. 12 refs.

The author has written this paper as the first of two designed to show that primary abdominal tuberculosis is a diagnosis too frequently made and often on insufficient grounds [presumably his observations apply mainly to India]. Among the signs and symptoms in the symptom-complex described are: discomfort or dull pain in the abdomen, sense of fullness, diarrhoea/constipation, anorexia, anaemia, loss of weight, possibly slight pyrexia, vague abdominal tenderness, especially round the umbilicus or in the right iliac fossa. No masses are palpable, and the abdomen is seldom doughy. The lungs are clear, and there are no foci of tuberculosis elsewhere. Females are more often affected than males,

and the patients are usually between the ages of 15 and 45. Attacks of " dysentery " may have occurred before. The author believes that abdominal tuberculosis secondary to pulmonary disease is common, but agrees with various authorities that the primary type is rare. He quotes Hurst's view that intestinal tuberculosis of hyperplastic type should be included in the group of regional ileitis. Both the intestinal and peritoneal types are generally secondary, and even abdominal glandular tuberculosis, except in children, is common only with the intestinal variety.

The author states that the following conditions should be kept in mind in the differential diagnosis: mucous or catarrhal colitis (often following badly-treated bacillary dysentery); amoebic colitis, non-specific enterocolitis (often after mal-use of purgatives); ulcerative colitis; spastic colitis; chronic appendicitis; malignancy; chronic Fallopian tube and ovarian infection; regional ileitis; sprue and coeliac disease; pellagrinous diarrhoea. It is stressed that bacillary dysentery, chronic amoebic dysentery, and misuse of purgatives are all common in India.

Various symptomatic and specific lines of treatment are indicated, among the recommendations being calcium gluconate for diarrhoea, " fresh curds " in place of milk, which is usually poorly tolerated, sulphaguanadine to disinfect the intestinal tract, and the daily use of isotonic low-pressure enemata (2 drachms (7 ml.) of sodium chloride and 1 drachm (3·5 ml.) of sodium bicarbonate in 2 pints (1·1 litres) of warm water). Six reports of adult cases that responded to the treatment are given. All the cases had been diagnosed as cases of abdominal tuberculosis.

[The author agrees that primary abdominal tuberculosis does occur in India, and his aim is to discourage loose diagnosis, especially, it would seem, in adults. In England the condition is fairly uncommon, and occurs mainly in children.] *J. V. Hurford*

2008. **Primary Tuberculosis of the Skin in Infancy.** (Tuberculosis primaria de la piel en la infancia. Sobre nueve casos clínicos)
T. Valledor, R. Rodríguez Gavaldá, and A. Fernández Baltrons. *Revista Cubana de Pediatria* [*Rev. cubana Pediat.*], **18**, 336–366, June, 1946. 20 figs., 39 refs.

According to the authors primary tuberculous infections of the skin are always preceded by skin injury—circumcision, cuts, piercing of the lobe of the ear—or by inflammatory manifestations—impetigo, eczema, pyodermatitis, or furunculosis. After the injury or inflammation has healed, followed by a " free interval " of a week or a fortnight, a nodule appears on the site of the original lesion and ulcerates. After a further 3 to 4 weeks the regional lymph nodes swell painfully and break down. Concurrently the temperature rises, with anorexia, anaemia, and loss of weight. Histologically the corium shows infiltration by neutrophil leucocytes, epithelial cells, and lymphocytes, and a necrotic zone with giant cells. During the acute phase bacilli may be discovered; they are not usually found at later stages. Children with primary tuberculous skin lesions—those with no pulmonary or other lesions—come usually from healthy families, while those with secondary skin infection come from tuberculous families. " Coincidence of erythema nodosum in contacts demonstrates primary infection." Primary infections of the skin are accompanied by massive lymphadenitis with subsequent fistulation; the lymphadenitis in secondary infections is more discrete and has less tendency to fistulation. Cure is usual after 2 to 3 years, but large scars remain. Treatment consists in absolute rest during the acute phase, and rest as needed during the allergic phase, accompanied by suitable feeding. In 2 cases small doses of sulphanilamide, amount not stated, were given with doubtful results. The authors describe 9 cases of primary tuberculous skin lesions in children from 2 to 11 years old. *M. B. Klein*

2009. **Comparative Study of Cutaneous Reactions to Tuberculin and BCG Cultures.** (Estudio comparativo de las reacciones cutaneas a la inyeccion de tuberculina y de cultivos de BCG)
F. Civeira and R. de Urioste. *Medicina* [*Medicina, Madrid*] **14**, 175–178, Sept., 1946. 14 refs.

Intradermal tests with tuberculin and with a corresponding preparation of B.C.G. were performed on 18 tuberculous patients. The tests started at a dilution of 1 in 1,000,000 and the concentration increased tenfold each time until a positive reaction was obtained.

There is no correlation between the sensitivity to tuberculin and that to B.C.G. *G. Discombe*

2010. **Minimal Tuberculosis in the Negro. A Study of Negro Patients Discharged from Robert Koch Hospital with Minimal Tuberculosis between 1927 and 1942**
S. S. Romendick and A. A. Bonner. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 97–103, Aug., 1946. 4 refs.

The authors state that they are " not totally in accord with the concept " that tuberculosis in the Negro is a fulminating disease. They therefore attempted a follow-up of cases of minimal pulmonary tuberculosis in Negroes, and present a survey of 52 patients discharged from the Robert Koch Hospital between the years 1927 and 1942.

There were 2 deaths, but in neither was the lung condition the immediate or even contributory cause. Only 19% of the cases were re-admitted to a hospital because of re-activation of the disease, which was then classed as moderately advanced. Of the group as a whole 25 were females and 27 males, and the mean age incidence was 25 years for the females and 29 for the males. In 36% there was a family history of tuberculosis, and in 50% the sputum was positive on admission. Fourteen, or 26·9%, had extrapulmonary tuberculosis, and 20, or 38·4%, had associated non-tuberculous disease; among these there was no instance of re-admission for tuberculosis. The percentage gainfully employed before admission was 71; reactivation of the disease after discharge was almost exclusively (90%)

limited to the group of manual workers. Treatment for 90% consisted of rest in bed only; the remainder had preliminary rest in bed followed by either a phrenic operation or a pneumothorax. Duration of stay in the sanatorium was longer than is usual for a comparable series of cases (40% for 1 to 2 years), and the authors consider that this prolonged period of hospital care is a significant factor in the obvious stability of the cases. When the patients were discharged the condition was arrested in 67%, apparently arrested in 5·8%, and quiescent, improved, or unimproved in 29%. It is of interest to note that of those who left hospital with the full approval of the staff (78·9%) only 15% required re-admission, whereas of those who left of their own volition (21·1%), 40% required re-admission.

Richard D. Tonkin

2011. **A Simple and Practical Method of Obtaining Complete Bronchograms**

J. K. POPPE. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 104–110, Aug., 1946. 5 figs.

A method of obtaining complete bilateral bronchograms on ambulatory patients on two *x*-ray films within half an hour is described. The three fundamental principles laid down are: (1) adequate anaesthesia; (2) avoidance of any delay between the injection of the oil and the taking of the film; (3) maintenance of constant traction on the tongue until the film has been taken. Soluble phenobarbitone 0·1 g. is given 2 hours before the bronchogram, and codeine 0·065 g. 15 minutes before the bronchogram. Postural drainage is employed for the half hour immediately preceding the injection of the opaque oil. The throat and larynx are sprayed with 1% butethanol; 30 ml. is used over a period of 15 to 20 minutes, the tongue being held out and the patient breathing through the mouth. The patient then sits in front of the fluoroscope and leans on his right or left elbow. The oil (10 to 12 ml. of 40% lipiodol, warmed) is slowly dripped from a straight metal cannula over the back of the tongue. The patient should breathe at approximately 30 times per minute, and the original position should be maintained for from 30 to 60 seconds after the injection. Filling is checked with the fluoroscope, the bronchi being filled when the patient is placed on the affected side and rolled slightly forward (middle lobe bronchus), while the foot of the stretcher is raised to 45 degrees for 30 seconds (upper lobe bronchus). The radiograph is taken in the posterior semi-oblique position, with the patient standing up with his arm on his head. Traction on the tongue must be maintained until the films have been taken. *Richard D. Tonkin*

2012. **Bronchography in Tuberculosis. A Clinical Study**

L. B. BOYER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 111–121, Aug., 1946. 4 figs., 19 refs.

In this investigation bronchography was performed on 46 patients, aged 16 to 75, 4 of whom were men and 42 women. They all showed different degrees and types of pulmonary tuberculosis. The method used was intratracheal intubation with a No. 12 or 14 French catheter, and introduction of the opaque oil under direct fluoroscopic vision. An attempt was made to inject into the area involved by the tuberculous process only. In most instances iodized oil was used, but in a few thorotrast was employed, as it is less viscid. There were some reactions. In 3 patients who had suspected bronchial stenosis thorotrast was used and the procedure was followed by a severe febrile reaction persisting for 2 or 3 days. In the others iodized oil was employed; there was a severe reaction in 1 case, with advanced bilateral disease; in 4 there was a moderate reaction; and in 7 mild disturbances. There were no instances in which any spread of the disease could be definitely attributed to the procedure.

The results are presented in detail. Bronchiectasis was demonstrated convincingly in 85% of the fibroid, in 36% of the fibro-caseous, but in none of the exudative types of the disease. Collapse therapy apparently bore no relationship to the incidence of bronchial dilatation. As regards bronchostenosis, of 30 patients in whom there had been a previous diagnosis on clinical grounds of tuberculous tracheo-bronchitis, 36% were proved to have stenosis, and 60% enlarged bronchi. In 16 cases in which the bronchi were considered to be normal, 6% were stenotic and 50% dilated. In the case of tension cavities (8 instances), 3 lobes showed both bronchiectasis and stenosis, 2 stenosis alone, and 3 neither. Bronchostenosis was always associated with a positive sputum, as was bronchiectasis in the majority of instances. The mechanism of production of bronchiectasis is discussed, and the conclusion is reached that it may be the result of fibrous pulmonary changes superimposed upon alterations of the bronchi caused by infection, since with the increase of pulmonary fibrosis following bronchial infection the incidence of bronchial dilatation sharply increases.

The author thinks that in the past the dangers of the procedure in cases of tuberculosis have been overemphasized; he does, however, discourage the use of thorotrast. One disadvantage is that subsequent radiography may be obscured for a varying period, in exceptional cases up to three years. He concludes that contrast bronchography is not a worth-while routine procedure in the management of pulmonary tuberculosis, but that there are certain indications for using it: (1) in cases where ordinary radiographs fail to reveal the source of a positive sputum; and (2) in hospitals where facilities for tomography are not available.

Richard D. Tonkin

2013. **Oleothorax. A Reevaluation—With a Final Report of 101 Cases**

R. H. BROWNING, E. S. RAY, and L. ROTENBERG. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 122–127, Aug., 1946. 2 refs.

In 1941 Browning and Ray reported a series of 101 cases in which oleothorax was used in the treatment of tuberculosis. The treatment was classed at that time as successful in 75 of the cases. A follow-up study of these 75 cases is now presented. Seventy patients were traced. Of these 14 developed complications; 8

bronchopleural fistula (5 fatal), and 6 recurrent empyema. Of the total 61·5% have been converted to pneumothorax with an attempt at re-expansion of the underlying lung; 18·5% have been continued. The reason for conversion was in most cases the fear of late complications, but in a few cases it was carried out because the period of collapse was considered to be adequate. Complete re-expansion was attained in 37%, " was probable " in 14%, and was not possible in 42%. Obliteration of the pleural space was not achieved in any case where the duration of oleothorax was more than 6 years. While many of these patients with unexpandable lungs are alive and working, they cannot be considered to be healthy.

The following observations, based upon study of the cases over a period of time, are made. (1) The incidence of complications increases the longer the oleothorax is maintained, the most serious of these being bronchopleural fistula. (2) Safe medical follow-up becomes increasingly difficult, but without it there may be disastrous results. (3) Conversion to a pneumothorax was followed almost universally by a recurrence of fluid; it was concluded that where the re-expansion is required it is better to permit the pleural space to fill with fluid and not to add more air. Periodical closed aspiration is employed to the point of discomfort.

In the original series there were two indications for the oleothorax: (*a*) obliterative pleurisy, and (*b*) a persistant tuberculous empyema. The authors now feel that the former is no longer an indication, and that thoracoplasty is the procedure of choice for the latter. Oleothorax should be considered only in cases which are not reasonable surgical risks. They make the following suggestions for minimizing the occurrence of tuberculous empyema: (1) All artificial pneumothoraces which cannot be made mechanically satisfactory should be promptly abandoned; (2) they should be abandoned early in the presence of effusions; and (3) induction of artificial pneumothorax should be avoided in the presence of acute exudative disease. *Richard D. Tonkin*

2014. **Dietaries in Tuberculosis Sanatoria. Report of the Approximate Nutritional Evaluation of Thirty-Four County Tuberculosis Hospital Dietaries during 1943 and 1944**

J. SEDGWICK. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 128–132, Aug., 1946.

The diets in 30 tuberculosis hospitals in the State of California were studied during 1943 and 1944. The standard arrived at was the daily allowance for sedentary man, recommended by the Food and Nutrition Board of the National Research Council, with the addition of protein and ascorbic acid. The outstanding deficiencies were found to be in calories (30% of the hospitals) and protein, thiamine, niacin, and ascorbic acid (50%). A high milk diet was general, and supplied a high intake of calcium and riboflavin. Preparation of food was found to be poor in 4 hospitals, fair in 9, and good in 17. It is pointed out that there may be an adequate daily menu in relation to specific nutrients, but poor preparation, such as destruction in cooking of heat-labile and water-soluble vitamins, may render it inadequate. " Variety, colour, and flavour " are stated to be important in the menus of tuberculous patients, who remain in hospital a long time; often it was found that insufficient care had been taken in this respect. Whole-grain cereals and high vitamin juices, fruits, and vegetables are advised as a substitute for milk, which in large quantity becomes monotonous and takes away the appetite of the patient for more solid food. It is recommended that there should be established a fairly accurate method of determining the approximate nutritive value of diets served over a period of time, and that it might be desirable to provide a consulting dietitian or nutritionist.

Richard D. Tonkin

2015. **Tuberculous Pleurisy with Effusion. A Manifestation of Extrapulmonary Tuberculosis**

E. G. JONES and M. DOOLEY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 133–139, Aug., 1946. 2 refs.

This study concerns 144 patients (106 negro, 38 white) admitted to Baltimore City Hospital, whose disease was diagnosed as tuberculous pleurisy with effusion without any pulmonary parenchymal lesion. Ages varied from 13 to 62. During their first stay in hospital extrapulmonary tuberculous lesions occurred in 20, and in 6 more later; of these, 23 were negro and 16 were known to have died. Of the total, 99 were followed up for more than a year or died of tuberculosis; 16 developed pulmonary tuberculosis (13 died). Proportional mortality was greatest in 9 patients with bilateral effusion, of whom 5 died of tuberculosis. Of patients discharged as arrested and followed up, 10 relapsed and 61 remained well.

It is claimed that pleurisy with effusion is often " a manifestation of widespread extrapulmonary tuberculosis ", especially in the negro of the Baltimore district, probably a racial characteristic. A bilateral pleural effusion generally means that there is also widespread tuberculosis elsewhere. As reactivation occurred usually within 2 years and chiefly among those discharged after only 2 or 3 months in hospital, pleurisy with effusion should be treated with as much rest in bed as any other form of acute tuberculosis and should be followed up for at least 2 years. Removal of pleural fluid may be necessary to facilitate a diagnosis of underlying lung lesion.

[This is an interesting short article. It might be of value to know in what proportion of the cases enlarged hilar nodes or other evidence of recent primary infection occurred, as in so many instances effusion, extrapulmonary lesions, and even pulmonary tuberculosis occur in the early post-primary phase.] *J. V. Hurford*

2016. **On a Metabolic Product of *Ps. pyocyanea*, Pyolipic Acid, active against Mycobact. Tuberculosis.** [In English]

S. BERGSTRÖM, H. THEORELL, and H. DAVIDE. *Arkiv for Kemi, Mineralogi och Geologi* [*Ark. Kemi. Min. Geol.*] **23**, A, No. 13, 1–12, 1947. 1 fig., 20 refs.

2017. **Tuberculosis as an Occupational Hazard during Medical Training. Report of a Case-Finding and Follow-Up Study, with an Effective Control Program for Tuberculosis in Women Medical Students**
S. I. MORRIS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 140–158, Aug., 1946. 33 refs.

This interesting and suggestive paper is a report on the working of a case-finding and follow-up programme for study of tuberculosis in students at the only women's medical school in America. The first plan, presented in 1932 and detailed in the article, provided adequately for the detection of the onset of both infection and disease, and set down precautions to be taken by those students who became tuberculin-positive and the steps to be taken to dispose of those developing an active focus. Unfortunately, certain factors interfered with perfect fulfilment of the scheme, especially in the early disposal of cases with active disease, though many had been corrected by 1944, when Mantoux-testing on non-reactors and filming of all students were being done biannually.

It was found that positive reactors increased in each class as it passed through the medical course; in fact, it became 100% by the autumn of the fourth year. For instance, among students who entered in 1932 the proportion of reactors in the autumn of the first year was 34%, second year 48%, third year 80%, fourth year 100%; this despite the fact that over the period up to 1944 there was a gradual reduction in the percentage of positive reactions in new students. The most rapid increase in infection occurred in the second half of the second year, and this was attributed largely to inadequate precautions in the post-mortem room. Out of 449 medical students in 12 years 56 developed definite active disease, 43 while still at college. The series supports the claim that recent sensitization predisposes to early disease, as shown in the following table:

Tuberculous Disease following Conversion to Tuberculin-Positivity

Number of cases observed	Development of demonstrable active tuberculosis after tuberculin conversion to positivity			
	Within 6 months	Within 12 months	In 12 to 18 months	In 2 years or more
38	22	12	2	2

The author concludes that as long a time as possible should elapse between Mantoux-conversion and exposure to tuberculous patients. [In other words, she supports the theory that disease arises from repeated "doses" rather than progression from primary infection.] A number of students showing *x*-ray evidence of "healed primary disease" but tuberculin-negative were "re-converted" during the course. In addition to the 56 definite cases, a further 19 students did not progress beyond a minimal suspicious stage.

The importance of early rest treatment for the early case is stressed, as is careful watching of the minimal lesion. One factor responsible for delay is the frequent masking of the early lesion by a clinical picture of upper respiratory disease, and *x*-ray evidence may even be attributed to "chronic sinusitis". Upper respiratory disease combined with fatigue and strain to cause the most frequent appearance of active disease at the end of the college year. Those infected during the pre-clinical period did not usually develop disease till the clinical period of the course. Class-room infection was shown to occur through retained or returning active cases infecting other students, and disease was found to be acquired also from contact with residents in extra-mural living-quarters.

[The author makes a number of other important points, and the paper is well worth reading in full. Her plea for an adequate control programme in medical schools and hospitals is a strong one, though one cannot but feel that the high disease rate in her series must be very exceptional.] *J. V. Hurford*

2018. **Tuberculin Reactors. An Interpretation and Evaluation of Certain Data**
H. H. DASH, A. R. MASTEN, C. F. TAYLOR, and O. S. LEVIN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 159–165, Aug., 1946. 8 refs.

This article evaluates tuberculin-testing with the assumption in mind that tuberculin is a *relatively* specific agent only. The stronger doses are said to give non-specific reactions in adults, but no strengths yield 100% positive results in cases of diagnosed tuberculous disease. After quoting various surveys, the authors conclude that the yardstick for the test is its reliability in tuberculous disease rather than "the meaningless reliability based on high numbers of reactors". If the test be employed diagnostically in case-finding surveys it should (*a*) approximate to 100% positive in cases of active tuberculosis; (*b*) give a minimum of reactors among persons without disease; (*c*) fulfil conditions of ease of administration, readiness of interpretation, and cost. The surveys reviewed are based on the use of either purified protein derivative (in various strengths) or a transcutaneous test, as described by Corper (*J. Lab. clin. Med.*, 1944, **29**, 398). A table (based on 5 authorities) from the article shows a comparison of reactors and tuberculous disease picked up by the different techniques.

Method	Reactors: %	Tuberculous disease: %
P.P.D.$_1$ (0·00002 mg.)	11·7	75
P.P.D. intermediate (0·0001 or 0·0002 mg.)	11·6–13·7	95
P.P.D.$_2$ (0·005 mg.)	43·3	95
Transcutaneous	9·8–19·9	95

On the other hand, if a test is designed to screen persons who may have a tuberculous infection but no verifiable disease it should: (*a*) detect to a high degree the specific tuberculo-allergic individuals; (*b*) give a minimum of non-specific reactions. It is stated that no intracutaneous test meets these conditions, though P.P.D. is much less

likely than O.T. to give non-specific reactions. The P.P.D.$_2$ dose of 0·005 mg. will, however, produce a high number of non-specific reactions, and the intermediate dose is preferable even when screening reactors. Moreover, the danger of severe reactions is always present with the use of initial doses of P.P.D. larger than 0·00002 mg. Long and his collaborators (who first described purified protein derivative: *Tubercle*, 1934–5, **16**, 304) are quoted as saying: " It is obviously impossible to determine in living human beings if any type of tuberculin is a perfect detector of tuberculous infection."

J. V. Hurford

2019. **History of H37 Strain of Tubercle Bacillus**
W. STEENKEN and L. U. GARDNER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **54**, 62–66, July, 1946. 1 ref.

Strain H37, perhaps the most widely used of all strains of *Mycobacterium tuberculosis* for research work, was isolated by Baldwin in 1905 from the sputum of a 19-year-old male patient suffering from chronic tuberculosis. It was first grown on a Hess agar plate enriched with cow's serum, and after the first generation was transplanted on to various solid media enriched with serum, meat extract, or egg. It was subcultured in this way until 1917. For the next three years (1917–20) it was grown on glycerol beef broth and glycerol agar. Then in 1920 a collateral line of culture was established upon the synthetic medium of Proskauer and Beck. Numerous publications by Baldwin, Krause, and Paterson during these years led to many requests for subcultures of the strain, and it was distributed to laboratories far and wide. Until 1922 subcultures of the original culture maintained in the Saranac Lake laboratory remained fully virulent for guinea-pigs, but at the end of that year the strain began to show signs of diminished virulence, and it was discarded in routine experiments. At the end of 1929, however, it was again used in conjunction with coal and silica dust for a series of pneumoconiosis experiments, and found to be of less diminished virulence than had been assumed. Silica could, in fact, stimulate its activity. From 1930 until 1940 H37 was not used at all for experiments on virulent infections in the Saranac laboratory.

Meanwhile, during the period 1922 to 1926 other laboratories to which the culture had been given also reported that the strain was fluctuating in virulence. Saranac Lake laboratory therefore proceeded to inquire into this rather abrupt change in the behaviour of a strain which had for some 22 years consistently maintained a uniform degree of virulence. A review of the cultural history of the organism showed that a change from Witte's to Fairchild's peptone was made about 1922. It had been noted at the time that broth made with the latter yielded a black precipitate which settled out of the fluid and had to be removed by filtration through a Berkefeld filter. It seems conceivable that in the process essential nutrients were removed from the broth or that the concentration of salts was altered. Fortunately a collateral line of culture had been established at the clinical laboratory at Trudeau Sanatorium where the synthetic medium of Proskauer and Beck containing no peptone had been used; a comparison of these two collateral branches of the strain suggests that dissociation of colonies may have taken place. The authors say: " Since the predominating colony in plate cultures of H37 and other strains previously grown for long periods on glycerol broth has the structure of a virulent dissociant it would appear that continued transplantation on this medium may ultimately result in the persistence of nothing but such mutants ". Whether the substitution of the new brand of peptone, however, was responsible for the sudden loss of pathogenicity still remains a mystery. Pending further research the authors have decided to abide by empirical experience and rely upon the synthetic medium of Proskauer and Beck for maintenance of virulence of stock strains. This virulent dissociant will now be among the strains maintained by the Culture Depot of the National Tuberculosis Association for distribution to investigators in the fields of chemotherapy and other research.

S. Roodhouse Gloyne

TYPHOID

2020. **Observations on the Treatment of Typhoid Fever.** (Osservazioni sulla terapia del tifo)
A. SERENA. *Giornale di Clinica Medica* [*G. Clin. med.*] **27**, 508–516, July, 1946. 2 figs.

The author [writing in September, 1942, when both sulphathiazole and penicillin were unknown in Italy] claims that vaccine therapy is the only really effective treatment of typhoid fever. At that time it had just successfully passed the experimental stage and was being put into practical use widely throughout the country. There is no agreement as to the mode of action of typhoid vaccine, most authors stressing the importance of the pyrogenic action, while others maintain that immunological responses produce the greater curative effect.

The author used vaccine treatment in the majority of 126 severe and moderately severe cases of typhoid admitted to hospital in 1941; vaccine was withheld only when the patient was admitted obviously *in extremis*. Hypertoxicity, cardiac or renal damage, and pregnancy were not considered contraindications; on the contrary, such cases stand one or more controlled shocks at reasonable intervals better than the continuous toxaemia of prolonged illness. The author maintains that treatment should be given as early as possible. In the few cases seen in the first week, with fever and a positive blood culture, resolution took place by crisis after 2 injections. Most of the patients, however, were admitted on the tenth to the twelfth or occasionally up to the eighteenth day of illness; symptoms such as headache, insomnia, and restlessness disappeared after the first injection, and usually about 7 injections were needed to complete the cure. The fever normally settled by lysis; the severity of the rigor and the magnitude of the pyrexial response to the injection, however, did not depend on the previous temperature. The vaccine was given intravenously; in an average case 100 million organisms was given to start with, or in very severe cases 50 million. It was given regularly ever third day; after the initial dose of 100 million, the doses were 200, 300, 400, 600, 800, and

1,000 million organisms, and occasionally 2,000 million. Accessory and symptomatic treatment was not neglected. It included intravenous glucose saline in the more severe cases, with small doses of insulin. Strychnine was given orally in all cases. Sympathomimetic drugs were administered to combat the fall in blood pressure due to peripheral circulatory failure which sometimes followed protein shock, and " cardiazol " (leptazol) was used to stimulate the cardiac centre. The traditional milk diet was supplemented with rice and cereals, lemon, orange, and grape juice and preserves. No patient died as a result of the shock treatment. In all treated cases there was a very definite reduction in the duration of illness and of convalescence, and of the number of days in hospital.

[No case histories are given, but two charts are included showing the striking response of the fever in a severe and a moderately severe case to repeated injections of vaccine.] *E. G. Sita-Lumsden*

PROTOZOAL INFECTIONS

2021. **Malaria and Urticaria**
H. H. Golz. *Annals of Allergy* [*Ann. Allergy*] **4**, 293–294 and 298, July–Aug., 1946.

The author reports a case of malaria associated with generalized urticaria and angioneurotic oedema. The patient, a man aged 24 years, had four attacks of urticaria at 48-hour intervals; in the first three there was no rise in temperature, but in the fourth there was a typical mild malarial rigor with fever. *Plasmodium vivax* in small numbers was identified in the blood film. After treatment with mepacrine no further attacks occurred. The patient stated that he had had similar urticaria at the onset of his only other attack of malaria 8 months before.

The author suggests that the malarial parasite acted as an allergen when free in the plasma, and that the first 3 attacks of urticaria were associated with subclinical malaria, which failed to give rise to the usual signs and symptoms owing to the low degree of parasitization.

[The evidence for regarding the malarial parasite as the effective allergen in this case is indirect and not entirely conclusive.] *R. S. Bruce Pearson*

2022. **Granulomatous Lesions in Visceral Leishmaniasis.** (Sôbre a presença de lesões inflamatórias do tipo granulomatoso na Leishmaniose visceral humana)
L. Bogliolo. *Arquivos de Clínica* [*Arch. Clin.*] **3**, 186–191, Sept., 1946. 1 fig., 9 refs.

The author criticizes the accepted view that an absence of inflammatory lesions is characteristic of visceral (*L. donovani*) leishmaniasis in man (as opposed to animals). It is generally held that in man only a uniform diffuse reticulocyte hyperplasia in haemopoietic organs occurs, two exceptions to this being found in human skin lesions: (1) in the granulomata in fatal cases among Indians in endemic areas, in whom there was no other clinical evidence of the disease, and in untreated or inadequately treated cases; (2) in the cutaneous lesions of leishmaniasis from the Sudan. When examining specimens from cases of human visceral leishmaniasis in Italy he found in the liver not only hyperplasia of Kupffer's cells, but granulomatous formations resembling tuberculides and comparable to those seen in the intestine and liver of leishmanial dogs. He therefore challenges the present view.

The hepatic lesions examined showed circumscribed foci of 150 to 200μ in diameter, either in direct contact with liver tissue or demarcated by a few fine collagenous fibres. They were generally found in the biliary channels, but were also seen within lobules. They varied in number in different cases. Their structure, cellular content, and staining properties are described in detail and illustrated by a photomicrograph. Giant cells were not seen; Leishman-Donovan bodies were sometimes present in small numbers—a point of difference from the lesion characterized by hyperplasia of Kupffer's cells, where the parasites are numerous. They were relatively vascular and showed no degenerative changes; the adjoining healthy liver tissue exhibited no reaction. Nowhere else in the liver was there evidence of inflammation, and no cause for it, other than leishmaniasis, could be found in these cases. The author suggests that this is an example of the principle of Jadassohn-Lewandowski, that when infective organisms are found in large numbers, because of the lack of any destructive agent, the inflammatory reaction of the tissues is morphologically unspecific, whereas when they have been largely destroyed, and have in consequence liberated endotoxins or other constituents, the tissue reaction is of a granulomatous type. The presence of two distinct reactions in the same organ is attributed to varying rates of destruction of the infective agent. The rarity of the inflammatory reaction is attributed either to the absence of an exotoxin in *L. donovani*, or to its failure to act as a foreign body, or to its not producing any local sensitization and the consequent allergic reaction. The author discusses whether the rare cases of hepatic cirrhosis found in visceral leishmaniasis could be the late result of the inflammatory reaction he describes, but he dismisses the possibility.

[The number of cases observed is not stated.]
J. J. Keevil

2023. **Treatment of Kala-Azar with a New Antimony Compound (2,168 R.P.). Preliminary Results.** (Traitement du kala-azar par un nouveau composé stibié: le 2·168 R.P. (premiers résultats))
P. Durand, S. Benmussa, and M. Caruana. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **62**, 399–409, July 5 and 12, 1946.

Six cases of Mediterranean kala-azar were treated in Tunis with " 2,168 R.P." a new quinquivalent antimonial of French origin. The drug is stated to be the " antimonate of N-methylglucamine ". It contains 28·35% of antimony, and is used in 30% solution, which therefore contains about 0·1 g. of antimony per ml. The drug was previously tested upon laboratory animals and was shown to have very low toxicity. An intravenous dose of more than 100 mg. caused no ill effects in the mouse. The case histories of the 6 patients are reported in detail,

and tables are given of differential counts upon blood and bone marrow before and after treatment. The drug was injected intramuscularly on alternate days, the doses being 2 to 5 ml. for an infant of 14 months, 10 ml. for 4 children aged 4½, 5½, 5½, and 14 years respectively, and 20 ml. for an adult of 36 years. A course of 12 to 20 doses was given, and, in all cases except the infant, there was a second course 3 weeks after completion of the first. Temperatures returned to normal after the third or fourth injection, the spleen was reduced in size after the fifth or sixth in most cases, and leishmania parasites had disappeared from the sternal marrow at the end of the first course. Serological reactions took rather longer to return to normal. The blood and bone marrow pictures were improved in all cases.

Three of the patients had previously received full courses of " diamidine " (stilbamidine ?) which had caused only temporary improvement. One of these, a child of 5½ years, had an infection of 3 years' standing, and had also received previous treatments with other antimonials, including " neostibosan ". Another child, aged 4½, had relapsed after a course of " anthiomaline " (lithium antimony thiomalate) and a course of 20 injections each of 30 to 40 mg. of " diamidine ". No severe toxic effects were observed with 2,168 R.P., but on several occasions in the early stages of treatment general malaise with shivering, nausea, and a slight rise of temperature occurred on the evening after injection. The authors consider that these effects may have been caused either by the drug or by the disease. Excretion of the drug was very rapid and only traces of antimony could be detected in the urine 24 hours after injection in a normal subject. In kala-azar patients the excretion was a little slower, but was almost complete in 36 hours. The authors suggest that better results might be obtained by giving the drug daily in order to maintain the concentration in the tissues. Most of the cases described have not been observed long enough for definite conclusions to be reached as to the value of the drug, but the preliminary results are considered to be promising.

[This drug is similar to sodium stibogluconate, in that the antimony is joined through oxygen to a carbon chain bearing a number of hydroxyl groups. Antimony is not joined directly to carbon as in the corresponding phenyl stibonic acid derivative of methyl glucamine (" pentastib ") or in such drugs as " neostibosan ". Larger quantities of antimony have been administered to the cases reported in this paper than is usual. Thus the adult received 12 injections each containing 2 g. of antimony metal in 24 days, apparently without signs of intolerance.] *L. G. Goodwin*

2024. **The Management of Amebiasis**
M. M. KARL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **78**, 789–798, Nov., 1946. 23 refs.

2025. **Active Immunization Against Malaria.** (The Wellcome Prize Essay, 1946)
C. J. WILDMAN. *Military Surgeon* [*Mil. Surg.*] **100**, 1–13, Jan., 1947.

HELMINTH INFECTIONS

2026. **Intestinal Parasites Diagnosed at an Army General Hospital in the South Pacific**
M. ZARROW and H. RIFKIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 289–293, Sept., 1946. 16 refs.

This paper records the results of a survey for intestinal parasites based upon stool examinations in 4,529 Service patients who had spent up to 3 years in the various islands in the South Pacific area. The incidence of both protozoan and helminth infections was not significantly different from that recorded by other workers in this area, except that the present authors found a higher incidence of *Entamoeba coli* and hookworm, and a lower incidence of *Entamoeba histolytica*. The incidence of protozoan infection was: *Entamoeba histolytica*, 4·9%; *Entamoeba coli*, 25·1%; *Endolimax nana*, 19·4%; *Iodamoeba bütschlii*, 4·1%; *Giardia lamblia*, 1·5%; *Trichomonas hominis*, 1·4%; *Enteromonas hominis*, 1·2%; *Chilomastix mesnili*, 0·3%; *Isospora hominis*, 0·4%; and *Embadomonas intestinalis*, 0·4%. The incidence of helminth infection was: Hookworm, 13·2%; *Trichuris trichiura*, 2·4%; *Strongyloides stercoralis*, 1·5%; *Ascaris lumbricoides*, 0·7%; *Enterobius vermicularis*, 0·4%; *Hymenolepis nana*, 0·3%. Eggs of *Heterodera radicicola* were found in 6 cases, but without any associated clinical findings. A single case of taeniasis was discovered. In one case many larvae of *Strongyloides stercoralis* were obtained during biliary drainage. The recorded incidence of hookworm was high compared with that found in the United States. In those cases where adult hookworms were recovered from the stools the species was found to be *Ancylostoma duodenale*. It was found that six successive stool examinations were necessary before a negative diagnosis could be accepted, but the full number was not made in all cases. Multiple parasitic infections found included 142 double infections, 44 triple infections, and 9 quadruple infections. Four cases of infection with *Isospora hominis* were noted, in 2 of which no other parasite occurred; of these 2, one was symptomless while the other showed mild diarrhoea and enterocolitis. One case of intestinal myiasis due to a species of sarcophaga was found. Incidence of giardia infection was low, which may have been due to the fact that many of the patients had received mepacrine treatment for malaria. As the incidence of infestation with other intestinal flagellates was also low it is possible that they too are susceptible to mepacrine.

J. M. Watson

2027. **Hookworm Infections in Troops Returning from the Pacific**
H. MOST, J. M. HAYMAN, and T. B. WILSON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 347–350, Sept., 1946. 19 refs.

This paper records the incidence of hookworm infections in troops returning from the Pacific as disclosed by routine stool survey. Of 2,500 consecutive admissions to hospital from the Pacific theatre, 11·5% showed hookworm infestation, while by contrast the incidence of

hookworm infestation in 4,300 patients who had seen service only in the United States was 6·2%. The report deals in detail with 284 patients. Incidence of infestation acquired overseas was very low in the majority of patients and was rarely related to clinical hookworm disease. Increased incidence of hookworm infestation found in Service personnel returning from various Pacific Islands was largely due to *Ancylostoma* infestation overseas; the ratio of *Ancylostoma* to *Necator* infections acquired in the Pacific was at least 3 to 1. Tetrachloroethylene was less efficient in eliminating *Ancylostoma* than *Necator*, which may account for the persistently positive stools after repeated courses of treatment. The high proportion of *Ancylostoma* infestations in these Service men suggests the possibility of the introduction and establishment of this parasite in the United States. Multiple parasitism due to protozoa and other species of helminths was common in men returning from the Pacific. *J. M. Watson*

2028. **Löffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis). Report of Twenty-Six Cases**
D. O. WRIGHT and E. M. GOLD. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 303–312, Sept., 1946. 3 figs., 31 refs.

The object of this paper is to show that cutaneous helminthiasis may be one more aetiological factor producing Löffler's syndrome (transitory and often migratory pulmonary infiltrations with peripheral eosinophilia and absence or paucity of systemic manifestations). Creeping eruption (cutaneous helminthiasis) is characterized by serpiginous reddish burrows in the skin, chiefly on the exposed surfaces, caused by infestation with the larvae of *Ancylostoma braziliense* (hookworm of dogs and cats); it is endemic in the south-eastern coastal regions of the United States. The authors observed 76 cases of creeping eruption, of which 52 could be studied for a fortnight or longer. Löffler's syndrome developed in 26 of these cases. The diagnosis was made by repeated *x*-ray examinations of the chest. All patients were afebrile, except 8 who had secondary infection of the cutaneous lesion. Physical signs over the lungs were absent or minimal. Differential blood counts carried out every third day showed eosinophilia ranging from 1 to 51%, and examination of the sputum for eosinophil cells gave counts ranging from 0 to 90%. Negative results were obtained in 441 examinations of stools for parasites and ova, except for 1 case in which they showed ova of *Necator americanus*. In the 26 patients with Löffler's syndrome, 204 examinations of the stools revealed the presence of *Entamoeba coli* and *E. nana* in 1 patient each, and *Giardia lamblia* in 2 patients. The sedimentation rate was normal in all except 8 cases; out of these 6 had secondary infection of the skin, and in the remaining 2 the raised sedimentation rate coincided with the pulmonary infiltration but returned to normal before the infiltration had cleared. Intradermal tests with extracts of *Ascaris lumbricoides* and *Trichinella spiralis* showed positive results to one or both antigens in 75% of 57 patients tested. It is concluded that the pulmonary infiltrations "are caused by an antigenic response to the presence of either the larvae or their blood-borne exotoxin". Recognition of the pulmonary condition is important in order to avoid the erroneous diagnosis of virus pneumonia, tuberculosis, or sarcoid. The result of treatment of the cutaneous lesions, the radiographic findings, and the normal sedimentation rate are the most important diagnostic criteria. Treatment consists of the application by spray of ethyl chloride for 30 seconds daily over an area 4 to 5 cm. in diameter about the ends of the cutaneous burrows. *A. Schott*

INFECTIOUS DISEASES OF UNKNOWN ORIGIN

2029. **Relapsing Erythema Nodosum of Long Duration.** (Un caso di eritema nodoso recidivante a lungo decorso) G. TASSINARI. *Giornale di Clinica Medica* [*G. Clin. med.*] **27**, 484–493, July, 1946. 21 refs.

A rare case is described of erythema nodosum which had been recurring over a period of 20 years. The patient was a housewife of 60. Her mother had died of pulmonary tuberculosis at the age of 77. She had had two attacks of pneumonia previously. There was no history of asthma, urticaria, pruritus, or other allergic conditions. For 20 years she had suffered from attacks of erythema nodosum in the lower limbs, more frequently on the right side. Usually three or four tender reddish-purple nodes 1 to 3 cm. in diameter would appear around the ankle-joint, and often there would be pain in the ankles, knees, elbows, and fingers with pyrexia and headache. After the original attack there had been a period of freedom for 4 years; thereafter attacks occurred frequently, sometimes two or three times a year, and usually in early spring and autumn. On examination only a systolic murmur indicating a probable mitral lesion was found. A tuberculin test, during a remission, was negative. *X*-ray examination of the chest showed increased lung markings in the right infra-clavicular region and a little fibrosis. The right apex was not so well aerated as the left. The left lung showed an enlarged hilar shadow with a few fibro-calcareous nodes. No treatment was of any avail, and there was no response to salicylate or to adrenaline.

The differential diagnosis from Bazin's disease, which also tends to relapse over long periods, is discussed; the latter occurs in young people and the lesions ulcerate, leaving atrophic scars. In a discussion on the aetiology of erythema nodosum the author points out the well-known relationships to tuberculosis, rheumatic fever, and streptococcal infection. Some authors maintain that it may be an individual disease, analogous to the acute exanthemata. It may also be a reaction to infections such as scarlet fever, measles, pyaemia, typhoid, syphilis, gonorrhoea, leprosy, and lymphogranuloma venereum. Erythema nodosum occur in coccidioidomycosis, when it is accompanied by eosinophilia. Erythema nodosum is often the first sign of tuberculous infection. In 30 cases, Corelli found 83·3% with radiological lung changes, while 90% gave a positive reaction

to the tuberculin test. Walgren obtained positive skin reactions in 95% of cases. Leisch found pulmonary changes in 81%. A negative response to the tuberculin test is presumed to be due to "cutaneous anergy"; the test is sometimes negative in the arm, but positive in the vicinity of the erythema nodosum. Tubercle bacilli have occasionally been reported from the lesions. *X*-ray examination of the chest most commonly shows enlarged hilar nodes, with occasional parenchymatous infiltration. Skin lesions in all respects similar to erythema nodosum have been experimentally produced in patients who had had erythema nodosum by the injection of such varied substances as sera, streptococcal toxins, tuberculin, and distilled water. Thus the condition must in many cases be due to non-specific allergy, in which the precipitating factor is different from the sensitizing agent. Among drugs which may cause erythematous nodes are iodine, antipyrine, and sulphathiazole. The presence in many cases of increased capillary fragility may explain the occasional bruise-like appearance of nodes and provides a link with Schoenlein's purpura.

The author has managed to collect only 5 other cases of chronic relapsing erythema nodosum from the literature; these were variously ascribed to rheumatic fever, focal tonsillar sepsis, and tuberculous cervical adenitis. In his own case the seasonal incidence may have been related to the hypersensitivity to tuberculin noted in spring and autumn. Tuberculous aetiology is suggested by the family history and by the *x*-ray evidence of old-standing lung lesions. The initial attack of erythema nodosum was caused by a single episode, probably rheumatic, which may also have caused a mitral lesion; against this background of sensitivity the repeated release of small quantities of tuberculin from a focus in the chest probably produced the skin lesions by parallergy. *E. G. Sita-Lumsden*

2030. **Inhibition of Hyaluronidase by Sodium Salicylate in Normal Individuals.** (Estudios sobre reumatismo. III. La inhibición de la hialuronidasa por el salicilato de sodio en individuos normales)

F. GUERRA and J. ROBLES GIL. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **16**, 293–301, July 30, 1946. 1 fig., 4 refs.

This is the third article of a series of studies on rheumatism. In 1945 Guerra demonstrated in rabbits the inhibition of hyaluronidase by sodium salicylate and the ineffectiveness of sulphadiazine in preventing diffusion. He considered that hyaluronidase might be a factor in rheumatic fever, since it is present in all the tissues chiefly affected. It is also present in bacteria, such as human haemolytic streptococci. The enzyme hydrolyses hyaluronic acid and increases the diffusibility in connective tissue of the infective agent and its metabolic products. Its inhibition by salicylates helps to explain their action in rheumatic fever. This study is concerned with the measurement of this inhibition in normal subjects and a comparison with the results found in rheumatic individuals.

A sterile 1% solution of Evans blue in physiological saline was used as indicator. A 1% solution in physiological saline of hyaluronidase, obtained from bulls testicles, was centrifuged for 5 minutes at 2,000 revolutions a minute and only the supernatant fluid used. A 10% solution of sodium salicylate was injected intravenously in proportions of 2 g. of sodium salicylate to each 50 kg. of body weight. Thirty-six healthy subjects, divided into 6 groups, were tested: 2 groups of male adults, 2 of female adults, and 2 of children. Two tests were made in each forearm of each individual in the following order:

A. Intradermal injection, lower right forearm, 0·25 ml. of 0·9% sodium chloride with 0·25 ml. of Evans blue.
B. Intradermal injection, upper right forearm, 0·25 ml. of hyaluronidase with 0·25 ml. of Evans blue.
C. Intravenous injection of sodium salicylate and, after 15 minutes, an injection as in A above, in the left lower forearm.
D. Intravenous injection of sodium salicylate and, after 15 minutes, an injection as in B above, in the left upper forearm.

The spread of the indicator at the test sites was measured with great accuracy after 24 hours. The results of 36 readings showed that hyaluronidase with indicator B spread over an area three times as large as that obtained in the same individuals when hyaluronidase was omitted (A). Hyaluronidase with indicator injected after the previous exhibition of sodium salicylate (D) spread over an area 49·5% of that seen in B.

The concentration of sodium salicylate in the blood in these tests did not approach the minimum considered adequate for clinical purposes in the treatment of rheumatic fever. In discussing these results the authors conclude that diffusion is promoted by hyaluronidase in the human skin. Using a double-strength solution in rabbit experiments Guerra has obtained an area of spread twice as great as that now recorded in human subjects. In previous experiments he has shown that the inhibition of hyaluronidase is related to the amount of sodium salicylate given, the area of spread of the indicator varying in direct proportion. The variations between the human groups chosen for these tests are greater than those seen in rabbits, but this is explained by such factors as the increased immunity of adults as compared with children and the presence of male hormones in some groups—a factor favouring diffusion. The differences within groups are explained as due to natural individual variations of race, age, or immunity, which were not appreciable factors when the experiments were carried out on rabbits from the same litter and in all ways identical. In 3 individuals who were given sulphadiazine during the tests the hyaluronidase-indicator areas were rapidly decolorized, suggesting that sulphadiazine stimulates diffusion in connective tissue. In a case of rheumatoid arthritis both those areas with and without hyaluronidase were smaller than in the controls, and in both the stain was deeper, more persistent, and not appreciably affected by the exhibition of sodium salicylate; however, reactions seen in cases of rheumatic fever were more significant. In one early untreated case the injection of the dye and hyaluronidase caused a large and rapidly spreading area of discoloration; when the test was repeated after administering sodium salicylate the area was reduced by 60% and the dye remained

for a long time, becoming more concentrated and showing no tendency to spread. Two cases showing unusual ecchymotic and allergic reactions are also described.

J. J. Keevil

2031. **Statistics of Rheumatic Fever in Mexico City.** (Frecuencia de la fiebre reumatica en la ciudad de México. Estudio bioestadistico)

J. Robles Gil. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **16**, 311–335, July 30, 1946. 35 refs.

The author gives tables showing the incidence and prevalence of rheumatism in Mexico City in order to establish more accurate standards for its future investigation, and to stimulate official interest in a great social and economic problem. Morbidity was studied through the admission to three hospitals, the attendance at three special clinics, and the incidence in one infant and one juvenile group of apparently healthy subjects. A more representative cross-section of the population could not be taken owing to lack of official authority for such a sociological inquiry, the illiteracy of many of the subjects who would have been involved, and the lack of an adequate medical research team. Mortality was investigated through 1,000 post-mortem reports in the General Hospital, death certificates being regarded as statistically misleading. The diagnostic standard adopted was that of the New York Heart Association.

Tables 1 to 5 illustrate the various classifications, such as site or form of lesion, and activity, under which rheumatism may be recorded in Mexican hospitals at present, and are an index of the statistical difficulties involved in this study. Tables 4 and 5 compare its prevalence with that of other diseases; this varies from 1·61% of all cases in the infant hospital and 1·02% in the General Hospital to 35·57% in the Institute of Cardiology. The exact period under review is not stated. Tables 6 to 11 deal with the total and relative incidence in heart and rheumatism clinics and in consulting practice. In the out-patient clinic of the Institute 44·88% of the heart cases were due to rheumatic fever. In the rheumatism clinic the incidence of rheumatic fever as compared with other manifestations was 13·63%, while in consulting practice the corresponding figure was 8%. Among 1,000 apparently healthy girls, whose examination included radiography and electrocardiography (Table 12), there was an incidence of 0·8% of polyarthritis, cardiac lesions, or chorea. Among 340 young adults the corresponding figure was 0·88% (Table 13). Table 14 gives the high figure of 12·6% among 1,000 necropsies as showing rheumatic cardiac lesions; 27% of these lesions had not been detected clinically. Table 15 shows the marked variation in the incidence of rheumatic fever at school age in different countries, the Mexican figures being intermediate. Table 16 gives the incidence of cardiac lesions among students in universities in the U.S.A.

The relatively greater incidence in infancy and among females is remarked upon, but the author stresses the fallacies in arguing from the special groups under review to the general population when medical supervision and diagnostic standards may vary considerably. The total incidence in Mexico does appear, however, to correspond with that in the U.S.A. and in Britain, and cardiac complications in different age groups are of the same order as in the U.S.A. and other countries. He concludes that Mexico should be placed among countries with a high incidence of rheumatic fever, and considers that statistics would be more informative as regards total incidence if an aetiological diagnosis were insisted on in place of the present custom of classification under manifestations. He urges the need for electrocardiographic examination before a suspected rheumatic heart is passed as normal. In conclusion he discusses the impossibility of effective prophylaxis without better statistics, a more informed bureaucracy, and a more educated public opinion. *J. J. Keevil*

2032. **Reiter's Disease with Prolonged Auriculo-Ventricular Conduction**

W. Feiring. *Annals of Internal Medicine* [*Ann. intern. Med.*] **25**, 498–507, Sept., 1946. 2 figs., 7 refs.

Two cases of Reiter's syndrome (polyarthritis, urethritis, and conjunctivitis) are described in which serial electrocardiograms revealed transient prolongation of the P–R interval from 0·18 and 0·19 seconds respectively to 0·24 seconds. The heart appeared otherwise normal, although a faint localized apical systolic murmur was heard in both. There was no evidence of preceding pyogenic infection in case 1, but there had been a series of infective incidents in case 2, the last (cellulitis of the calf requiring incision and drainage) beginning 5½ weeks before the first manifestation of Reiter's syndrome (urethritis), and 9 weeks before the onset of polyarthritis. The significance of the prolonged P–R interval is doubtful. *Paul Wood*

2033. **Electrocardiographic Studies in Rheumatic Heart Disease with Reference to Interpretation of Multiple Unipolar Precordial Leads**

S. R. First, A. W. Stickle, and R. H. Bayley. *American Heart Journal* [*Amer. Heart J.*] **33**, 1–13, Jan., 1947. 8 figs., 12 refs.

2034. **The Duration of the Electrical Systole (Q–T) in Acute Rheumatic Carditis in Children**

L. M. Taran and N. Szilagyi. *American Heart Journal* [*Amer. Heart J.*] **33**, 14–26, Jan., 1947. 7 figs., 18 refs.

2035. **Rheumatological Equipment in U.S.A.** (L'equipment rhumatologique aux Etats-Unis)

J. Robin. *Presse Médicale* [*Presse méd.*] **55**, 118–119, Feb. 15, 1947.

2036. **The Prognosis in Different Types of Rheumatic Valvular Lesion.** (Prognosen vid olika typer av reumatiska valvefel)

N. Svartz and T. Ernberg. *Nordisk Medicin* [*Nord. med.*] **33**, 757–759, March 28, 1947. 1 fig.

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